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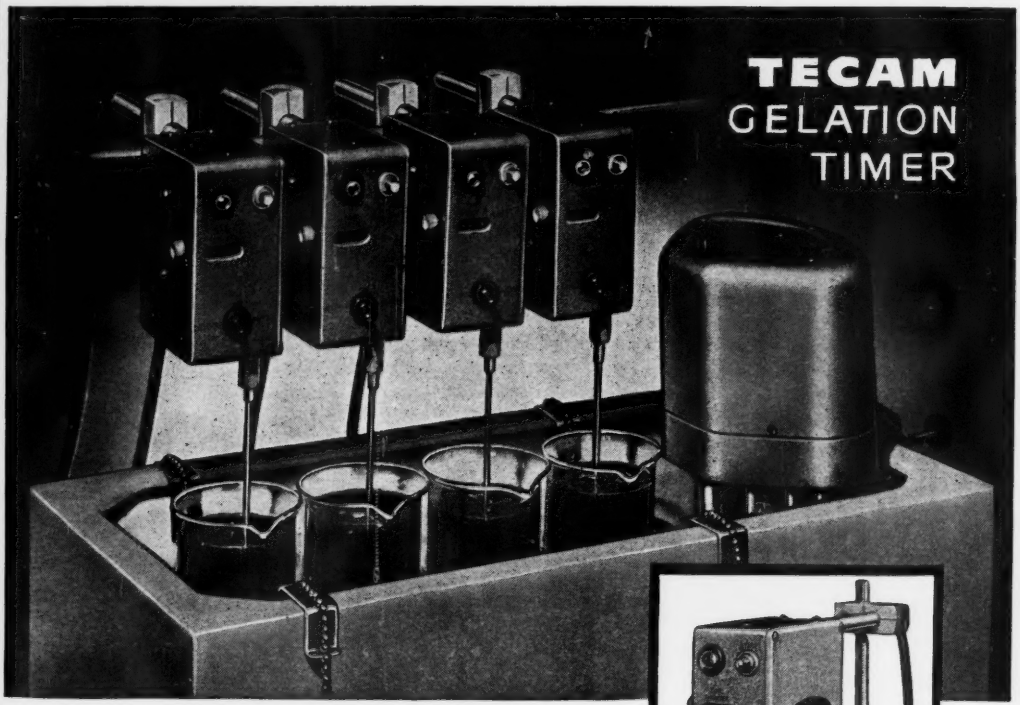

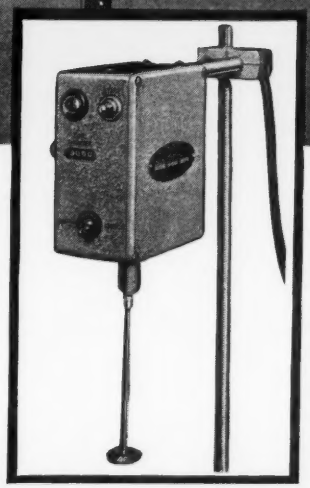

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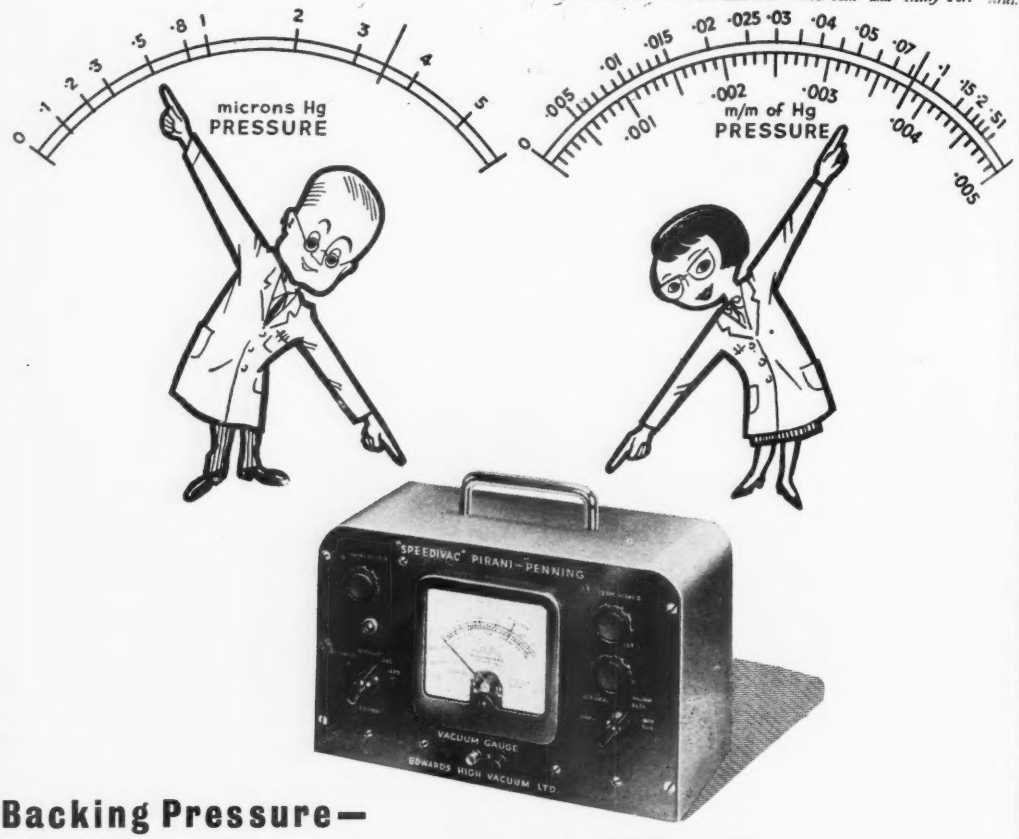

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SCIENCE AND SOCIETY

IN an address at the California Institute of Technology on June 12, the substance of which appears on p. 135 of this issue, Sir Solly Zuckerman remarked that the element of the unknown in government increases with every step we are now taking to apply the fruits of science, and that if, as some consider, sovereign power is being abrogated, it is not to some governing body, however formed, but more and more to a process of applying scientific knowledge without any real possibility of determining its final consequences. Dr. Brian Chapman closed his recent book, "The Profession of Government"*, with the remark that in the past hundred years in Europe arbitrary power has been replaced by anonymous power, and anonymous power is the antonym of public administration. It is, in fact, in the context of the problem of government that Sir Solly approaches his subject of liberty in an age of science, and the second main point to which he directs attention is that science, itself demanding freedom and revolutionary in its ways, is now determining, in an increasingly unpredictable way, the main issues about which citizens exercise their freedom of choice. This involves consideration of both the means and the purpose of government.

Sir Solly Zuckerman begins in a way which recalls Sir Charles Snow's Rede Lecture, and also Dr. P. A. Weiss's address, "The Message of Science", at Brussels last year, by discussing the divergence between the scientist and the humanist, quoting George Gissing's fear that science would become the remorseless enemy of mankind, before he goes on to explain the nature of science itself and of its dependence on freedom. For the scientist this means not only the freedom to choose his own problems to investigate, but also the fact that significant advances in scientific knowledge cannot be ordered by decree. Because scientific advance is unpredictable, "the untrammelled emergence of new scientific ideas is not compatible with any restraint on the liberty of the scientist to roam where his fancy leads. Indeed, once the growth of any set of scientific ideas becomes constrained, they are in danger of becoming obstructive dogma".

It is this freedom of science even to be revolutionary that raises doubts and even controversy if stability is to be achieved in a world in which the impact of science is so profound, and Sir Solly Zuckerman points that out; while the growth of fundamental scientific knowledge necessitates complete freedom from restraint, science is not uniquely associated with the preservation of freedom either in the personal or the social sphere. The applications of science have indeed provided the apparatus which has made central government powerful alike in a democratic and in an authoritarian regime. Science itself has no inherent moral direction, and while science will be the handmaiden of equality in the economic sphere, given the appropriate political institutions, our social environment is constantly being transformed by new scientific ideas and by the application and practical development of those ideas.

It is in this way that science helps to define for us the content and boundaries of the area within which we exercise our freedom; and in this sense only, the sense in which freedom was conceived by the utilitarians of the industrial revolution, science can be described as the handmaid of freedom. Through its practical impact, science to an increasing—almost to a dominant—extent is determining the way in which the sovereign power expresses itself, and here Sir Solly asks whether in choosing to regulate our lives in accordance with scientific discovery we know for what it is we are opting. "Is the sovereign power consciously deciding to develop this or that scientific discovery, and so to determine social development in this or that direction?"

The answer to any of these questions is inevitably bound up both with the constraints and the unpredictability of any major scientific advance. Moreover, as Sir Solly himself reminds us, scientific knowledge never develops evenly over the whole potential field of knowledge, and by choosing one out of several possible courses of action in search of a solution to a problem, the scientist may deny himself, and others, the opportunity of pursuing another. That applies still more to the choice of problems to be investigated, as the recent debate over Britain's decision to enter the field of space research should sufficiently illustrate, and beyond difficulties due to the increasing complexity of scientific knowledge and its application lies the impossibility of defining in advance the nature and magnitude of potential discovery or its impact on our social lives. Moreover, there may well be unforeseen and unexpected secondary social effects, as is well illustrated in Dr. Michael Young's discussion of possible effects of selection on the basis of intelligence tests in his book, "The Rise of the Meritocracy". Well may it be asked whether there can be much more than a fictional verity in the abstract idea that an area exists within which men can enjoy the capacity of unconditioned or untrammelled choice.

Sir Solly seems to recognize clearly enough that this is ultimately a problem of government rather than of philosophy. His remark that the only form of exploitation which democracy—man's answer to tyranny and exploitation—will never overcome is the coercion of new knowledge, which, by guiding our social lives into certain channels, limits advance in other directions, should be pondered in the light of the clear warning about the dangers of secrecy which Dr. Brian Chapman gives in his final chapter. Dr. Chapman is exposing the stupidity of secrecy from the point of view of relations between the

* The Profession of Government: The Public Service in Europe. By Dr. Brian Chapman. Pp. 352. (George Allen and Unwin, Ltd., 1959.) 28s. net.

government and the public. All that he writes, however, about the futility of the pathological secretiveness of the British Government, matched in Europe only in Spain and Portugal, applies even more forcefully where science is concerned. These attempts at secrecy merely hinder scientific or technical advance without promoting security and, more serious, impede the informed public discussion and understanding of what both science and Government are doing which is essential if science is to be wisely used.

This is even more important now that we stand at the cross-roads, as Sir Solly reminds us. Hitherto, we could claim that the applications of science have increased the sum total of human happiness. The process of applying scientific knowledge is as endless as is the prospect of getting new knowledge, and we can be reasonably certain that neither the backward and under-developed nor the rich nations will allow the process of applying the fruits of scientific knowledge to stop, either in the national or the international framework. In this process, however, means become ends, because as new ways of doing things are discovered, they transform the things done, and so their purpose. In fact, weapons may end by determining strategy and even the purpose behind the strategy.

Here, in Sir Solly's view, arises the real clash to-day between the scientist and the humanist, and this form of scientific application could indeed constrain our democratic liberties and even, if we ceased to be vigilant, the liberty of science itself. That would seem to imply a special responsibility for the scientist, though Sir Solly does not agree that such a responsibility means more than that the scientist is better able to appreciate scientific facts. It is not reasonable, he points out, to expect the scientist as such, who is not responsible for the application, to accept the responsibility for predicting some vast social transformation which might result from a seemingly innocent observation.

Nor is that all, for it has to be remembered that the process of government involves much more than taking account of scientific and technical factors and their implications. Even if the problem is essentially a scientific one, the statesman or minister who has to take a decision and formulate a policy must have regard to public acceptability, and accordingly to the public understanding. Normally there will be many other factors to be considered, and it is the consequences of the application of science that are of most concern, since they are most readily appreciated by the public and most relevant politically.

It is noteworthy that in this connexion Sir Solly Zuckerman reaches the same conclusion as to the importance of education as do Dr. Chapman and Mr. C. H. Sisson in another recent book on government*. Sir Solly suggests that in this problem of preserving our liberties lies the most important reason for regarding an education in science as constituting to-day an essential part of an education in the humanities. An understanding of social and political purpose can no longer be realized through the liberal arts, unless their scope is widened to embrace a proper understanding of the scientific knowledge the application of which is so rapidly transforming our intellectual and material environment.

It is with realism and not arrogance that Sir Solly places science, technology and humanism in that order of importance in determining our affairs; and in the same spirit that he suggests that, to continue as a potent educational discipline, the humanities must encompass an understanding of the social forces which arise from the application of the natural sciences. Nor does he suggest that higher education necessarily guarantees higher virtue or higher political wisdom; rather we are likely to avoid bad decisions if we realize that decisions taken in major scientific matters to-day may determine the course of the future. Dr. Chapman comments that no other European country has emphasized to the same extent as Britain the strange division between science and the humanities, with the result that the common difficulty of finding adequate numbers of Civil servants with sufficient specialized training is accentuated; nevertheless, he recognizes that all branches of the public service, ministries as well as industrial public enterprises, need a proper balance between administrator, manager and technician, and that ministries often lack technical competence in scientific, industrial and economic fields.

Apart, however, from referring to the way in which France has been able to meet some 90 per cent of her requirements for first-class engineers and technologists with administrative experience, Dr. Chapman does not discuss the place of the scientist or technologist in administration. He stresses the importance of education and recognizes that this means the education of the general public as well as of the administrator, and the politician and minister. He makes the significant comment that a menial mind should not be a qualification for high administrative office; but his constructive criticism is rather on the structure of the Civil Service itself, where it points to the fresh thinking that is required in order that the public services may be able to fulfil the needs of the modern State.

Nor are his suggestions for the Civil servant or the minister alone: they are no less worthy of the attention of professional organizations, for they point to ways in which not merely could the public services be absorbed more effectively into the structure of the modern State, but also, and no less important, the professional scientist or technologist could serve the State under conditions less likely to constrain professional ideas and tradition. Mr. C. H. Sisson, in "The Spirit of British Administration", is less confident as to the possibility of a general liberality, though he believes just as firmly as Sir Solly Zuckerman and Dr. Chapman that the survival of some kind of liberal and general education is indispensable to the survival of parliamentary

* The Spirit of British Administration and some European Comparisons. By C. H. Sisson. Pp. iv+162. (London: Faber and Faber, Ltd., 1959.) 21s. net.

government or indeed of any government based on free discussion; with this goes the survival of administrators who are not daunted by specialists but take it for granted that the practical implications of all their work can be explored and explained by a sufficiently agile lay mind.

The defence of freedom is a central problem of our time, and it is not simply one of defence against aggression from totalitarian systems outside. Sir Solly Zuckerman shows clearly how it arises from the nature of science itself, and from the impact of science on society. Any scientist or technologist who is concerned about those changes and how they can be best avoided or minimized will be led inevitably to think not simply about the association of scientist or technologist with government but about the process of government itself. To such thinking both the books mentioned above offer some contribution in different ways: they can assist in the understanding of the nature of administration and the limitations within which the administrator works; they indicate also the mind of the administrator and how it is trained or formed, and they point to some of the ways in which reform or developments are required if the task of government is to be discharged adequately to-day. But, like Sir Solly Zuckerman's address, they are primarily a challenge to the scientist or technologist to accept such responsibility to-day, and a stimulus to the creative thought by which alone that responsibility can be discharged.

THE NEED FOR MARINE RESEARCH

Living Resources of the Sea

Opportunities for Research and Expansion. By Dr. Lionel A. Walford. (A Conservation Foundation Study.) Pp. xv+321. (New York: The Ronald Press Company, 1958.) 6 dollars.

IT is more than sixty years since the foundation of the International Council for the Exploration of the Sea, the avowed purpose of which is the accumulation of knowledge necessary for the rational exploitation of marine resources in northern waters. There are now a dozen or more councils or commissions covering other areas of the world, including commissions limited to certain animals, such as halibut, salmon, tuna, and whales. The fear of over-fishing, which has been the spur to the activity of the International Council, the Halibut Commission, and other more recently formed organizations, has always been well to the fore in the minds of those concerned with the science of the sea. The necessary research has been concentrated on the main northern fisheries, but now the demand to feed the under-nourished millions has focused attention on the sea as a whole as a possible source of protein.

At the request of the Conservation Foundation, Dr. Lionel A. Walford, chief of the Biology Branch of the U.S. Fish and Wildlife Service, was asked to explore the question: "What scientific researches, apart from those which are in progress, would contribute significantly toward learning how to enlarge the yield of food from the sea in answer to human needs?" This has resulted in a useful book in which Dr. Walford considers the problem from human and biological angles. The major conclusion is that research must be extended into those areas where the need is greatest, and where there is the most possibility of increasing the food supply where it is most lacking. A number of interesting charts are included indicating the existing intensity of fishing and research in different parts of the world, those areas of the sea which might be expected to be productive, and those on land where the need for food is greatest. This survey impresses on us that where the fisheries are at present most developed and exploited there lies the major effort of research. The number of pertinent marine laboratories is now about 240. Nearly 90 per cent of these are in the northern hemisphere and 85 per cent north of latitude 20° N. Thus, those areas in which the need for research is now greatest have least facilities to do so both in material equipment and trained personnel. The problem is one both of research and development, and it is not easy to do the former without the latter unless exploration for fishing grounds is subsidized by governments.

It is thus both humanely and politically advisable that the countries most advanced in marine research should do their utmost to help the under-developed areas. Since the Second World War fisheries research under the auspices of Her Majesty's Colonial Office has added significantly to knowledge in certain areas, the U.S. Fish and Wildlife Service has extended its investigations into the oceanic pelagic fisheries, and the United Nations Food and Agriculture Organization has helped in supplying experts and supervising training. But this effort should if possible be much increased, and every encouragement given to those who wish to do research that will add to our knowledge of conditions in tropical seas.

Dr. Walford's book is not a text-book; it attempts to show where lie the gaps in knowledge, and these are both large and numerous. As a single example, what do we know of the probably enormous food potentialities available in pelagic cephalopods which now constitute 60 per cent of the Japanese fisheries?

Marine resources are also not necessarily all of value as food; some may have medical value. On our own planet there lies a whole world which we have only recently begun to study extensively. It is to be hoped that Dr. Walford's book may stimulate us to greater efforts. F. S. RUSSELL

ANOTHER DEBT TO DARWIN

Index Kewensis

Plantarum Phanerogamarum. Supplementum Duodecimum Nomina et Synonyma Omnium Generum et Specierum ab Initio Anni MDCCCCLI usque ad Finem Anni MDCCCCLV. Nonnulla etiam antea Edita Complectens, Ductu et Consilio Georgii Taylor, confecerunt Herbarii Horti Regii Botanici Kewensis Curatores. Pp. iii+157. (Oxonii: E Prelo Clarendoniano, 1959.) 75*s*. net.

IN this centenary year of the publication of the "Origin of Species" biologists have very much in mind the debt that they owe to Charles Darwin. It is probable, nevertheless, that many of them do not remember that the inception of "Index Kewensis" was due not only to Darwin's perception of the necessity for such a work but also to his generosity in providing the funds.

We might at this moment remember that the work was started under the supervision of Darwin's great friend, J. D. Hooker, and has since been supervised by subsequent directors of Kew and carried out by numerous able, but often anonymous, helpers.

"Index Kewensis" is taken so much for granted by plant taxonomists working with angiosperms that it is often not fully appreciated. To anyone who has struggled, even briefly, with taxonomic and nomenclatural problems in groups such as algae, where no such index exists, the lack of it is keenly felt and the value of a catalogue of names with places of publication is soon fully realized. It is interesting to note in this connexion that an "Index Muscorum" is due to be published shortly—another descendant of the original Darwinian idea.

"Index Kewensis", the twelfth quinquennial supplement to which has now been published under the direction of Dr. G. Taylor, supplies far more information about flowering plants and papers concerning them than might at first sight appear.

For example, in the five-year period between 1951 and 1955 approximately 12,000 species of flowering plants have been described. This, after more than two centuries of taxonomic work in the post-Linnean period, is a staggering total and gives some measure of the imperfection of our knowledge of the dominant group of plants.

It is also easy to obtain from these Supplements references to important monographs and information about the geographical areas and the plant groups which have been the subject of special attention in the recent past, as well as the names of the workers concerned.

In conclusion, I may perhaps be allowed to repeat what has so often been said before: "Index Kewensis" is indispensable. T. G. Tutin

OPTICS: CLASSICAL AND MODERN

Concepts of Classical Optics

By Dr. John Strong. Pp. xxii+692. (San Francisco: W. H. Freeman and Company; London: Bailey Bros. and Swinfen, Ltd., 1958.) 9.50 dollars; 80*s*.

THIS is a very good book, and one of its best features is the care taken by the author to ensure that the student understands what is going on. Mathematical treatment is kept to a minimum, but where it is necessary we are not left to flounder; the author explains what he is doing by means of a sort of running commentary, and even reassures us that although the solution we are after is buried in complication at the moment it is going to emerge safely in a minute. The only criticism here is that some simplification of the symbols used would lead to even greater clarity; for example, why was it necessary to use the symbol λ for mass early in Chapter 1, only to announce, a few pages later, that "we now abandon this for its customary use, symbolizing wavelength"?

The author also takes the trouble to expose and explain theoretical difficulties which are too often ignored. A good example of this is the section on "No Diffraction, by Cornu's Spiral", in which the limitations of this construction are pointed out, with the conclusion that "it affords the student an example of a typical theory in physics which has an impressive neatness, inspiring awe; which makes necessary compromises, requiring prudence; which is blemished by a lack of complete validity, requiring understanding".

At first glance the most distinctive feature of the book is the character of the illustrations. These are in the style one associates with the author's well-known book on laboratory practice. They have a freehand appearance, are pleasant to look at and are extremely clear; for example, the drawings in the section on double refraction, which is inherently a difficult subject to illustrate, are models of clarity. What is even more important is that the drawings showing apparatus give one a good idea as to how it is actually constructed—too often one's first sight of the actual equipment comes as a shock after having seen only text-book illustrations. It is only in some of the attempts to reproduce optical images by means of sketches that actual photographs might have been better.

The book is described in the preface as being intended for an intermediate course in optics, taking one or two terms. This is a considerable under-statement of the ground covered, and the book should be valuable for much more advanced students and also for general reference purposes. It in fact covers most of the physical optics required for an honours degree in physics.

The only real adverse criticism of this book concerns the price—£4—which is surely at least twice as much as most students would willingly pay for a single book. This is to some extent offset by the seventeen so-called appendixes, which occupy nearly half the book, and are in effect a series of short monographs by specialists. To quote the preface: "these are intended to give the student the flavour of current activities and interests in our field". The topics covered in this way include, among other things, interferometers, apodization, Fourier transformations and interferometric spectroscopy, radiation detectors, micro-wave optics, wave theory of image formation, lens design, fibre optics and filters. One of the appendixes supplies some of the mathematical background assumed in the rest of the book. This is well done, and includes frequent attempts to make the student think—both by formal examples and by interjected questions such as "(why?)" or "(how do we know?)" after mathematical steps in the text. J. E. Geake

BLOOD GROUP METHODS AND TECHNIQUES

Practical Blood Grouping

By Dr. F. Stratton and Dr. P. H. Renton. Pp. xxiv+331+16 plates. (Oxford: Blackwell Scientific Publications; Springfield, Ill.: Charles C. Thomas, Publisher, 1958.) 42*s*. net.

OVER the past fifteen years mass grouping of blood donors and ante-natal cases has grown enormously, and of necessity special methods and techniques have been evolved to meet an entirely new situation.

The authors of this book, faced with the alternatives of describing a multiplicity of methods, or confining themselves to those known and well tried in their own laboratory, have wisely chosen the latter.

Not all would agree that the papain slide test offers substantial advantages over existing (and equally well-tried) techniques, for example, tube testing. Even if some small advantage could be

demonstrated, the disorganization which would follow a drastic change to a new technique would carry inherent dangers, probably outweighing any benefits likely to result.

Nevertheless, it is always of value to study methods which have proved satisfactory over a number of years, and many pathologists engaged in this work will be most interested in a method which has satisfied such critical observers as the writers.

In the section dealing with ante-natal grouping, the possible alternative to the current practice of ABO and Rh(D) screening, with the customary follow-up of the Rh(D) negatives, is attractive from the point of view of economy in laboratory working. It might, however, be difficult to convince clinicians, and particularly obstetricians, that this economy at the expense of their advance knowledge of their patients' groups would be justified. It is certain that they would argue, as is foreseen by the authors, that obstetric emergencies would not be so well covered.

It would seem that the writers themselves have not adopted this possible alternative in their own practice, having doubtless explored the possibilities and the difficulties which it would entail.

An interesting and informative chapter on cross-matching difficulties encountered in their own laboratory (p. 237) was found to be slightly confusing. For example, of the 2,967 cases involved the donor's blood was not of the ABO group as stated on the bottle in two cases.

Without knowing the total number from which the 2,967 are selected the two wrongly labelled bottles may or may not represent a much higher proportion of error than is considered unavoidable in an earlier chapter.

In any event, some explanation of how these two bottles escaped the rigid checks and cross-checks, described in detail in Chapter 7, where the combined manipulative and serological sources of error are calculated at 1 in 43,000, would be helpful.

Two mistakes of this nature, picked up on cross-match, might represent a total of four such errors in the series, since bottles wrongly labelled O would escape detection by this final cross-matching check.

Minor points, such as these, and the confusion in the description of the anti-U antibody (p. 281) must not be allowed to detract from the value of this book. The subsequent editions, which will assuredly be demanded, will provide opportunity for elucidation and correction.

The bibliography is comprehensive and indicates the degree of care that has been taken in providing a manual which should appeal to pathologists, technicians and indeed to all engaged in blood transfusion work.

R. A. ZEITLIN

SCIENCE AND THE HUMANITIES

History and Philosophy of Science

An Introduction. By L. W. H. Hull. Pp. xi + 340 + 16 plates. (London and New York: Longmans, Green and Co., Ltd., 1959.) 25*s*. net.

"THIS is not a detailed history of science. It tries to bridge the gap between science and the humanities by considering scientific ideas in a context of history and philosophy." In these words the author describes the object of his work. Few will deny the existence of the gap, or the need to bridge it, and a book of this nature should be welcomed, on one hand, by those whose training and background have led to an emphasis on technology, and on the other, by students of the humanities who seek to understand the vital contribution of science to human thought. The general reader also will find the author's approach both interesting and stimulating; he anticipates the criticism that "most readers will, no doubt, find too little about some topics and too much about others". He points out that before the spread of evolutionary ideas the influence of biology seems scarcely comparable with that of mathematics and the physical sciences.

The book opens with a review of ancient science covering three periods: the first from the beginnings of science until the rise of Athens after the Persian wars; the second until the Macedonian conquests of the fourth century B.C.; the third period takes the Alexandrians as its theme. This review is comprehensive in relation to the hundred pages allotted to it, and makes interesting and instructive reading. Chapter 4 carries the story through the period of the Middle Ages, with some reference to Arabic contributions.

In the two following chapters, celestial geometry and celestial mechanics are very adequately surveyed from the time of Copernicus to that of Newton. With such fundamental changes in ideas concerning the universe, it is appropriate that a chapter is devoted to "Changes of Outlook and Method", and this constitutes one of the most valuable parts of the book. A separate chapter deals with other scientific developments in the sixteenth and seventeenth centuries, such as the phenomenon of light, and attention is directed to the philosophical thought of Berkeley and Hume.

The chapter "The Nineteenth Century and Evolution" introduces the reader not only to Darwinian theory and its implications but also to its significance in the development of thought. In an "Epilogue" which includes the theme of twentieth-century trends, the author gives a warning which it is to be hoped, in the interests of both science and the humanities, will not fall on deaf ears. "It is urgently necessary to restore the unity of intellectual life. Unless we do so, we shall soon lose what is best in Western civilization."

H. D. ANTHONY

INDIAN PREHISTORY

The Pre-historic Background of Indian Culture

By D. H. Gordon. (Sponsored by Bhulabhai Memorial Institute.) Pp. xi + 199 + 32 plates. (Bombay: M. D. Desai, 1958. Distributed by N. M. Tripathi (Private), Ltd., 1958.) Rs. 20.

UNTIL recent years the study of the archæology of the Indian peninsula has woefully lagged behind that of some other parts of the world. Especially is this so in the case of its prehistory. It is true that isolated finds of stone implements have been made from time to time during the past one hundred years—and in this connexion the name of Bruce Foote in Madras has an honoured place—but it is only recently that it has become possible to piece together an overall picture of the successive cultural phases in India, and even now the gaps in our knowledge are more than numerous. The subject is complicated since India seldom presented a uniform picture. Even in very early times the Madras area formed part of the vast Chelleo-Acheulean complex,

while the northern regions belonged to another and distinct province which included the early stone-age cultures of Burma and south-east Asia. Most of the worthwhile investigations have, until recently, been undertaken by non-Indians, but nowadays highly trained investigators like Dr. Sankalia and his colleagues have come into the field and are making important explorations. But there is so much to be done in the field that there is little opportunity for these investigators to stand back, as it were, and give a general report of what has so far been pieced together of the ancient history of their fascinating land. It is here that Colonel Gordon steps in.

Gordon has served, travelled and explored in India for thirty-two years and himself has undertaken not a few investigations, and he knows as much about the rock-shelter paintings of the Central Provinces as any man alive. But in the volume under review he has set himself the task of attempting to see the archæology of India as a whole and to make available for students the latest ideas on the subject. Geographically, India is a large and varied country, and just as the cultures are not, and never have been, uniform throughout, so the climate differs in different areas and has differed greatly in past ages. A brief study of climate changes must necessarily be considered first, and then the earliest stone age cultures can come under review. The later stone age cultures are next dealt with, and here it must not be forgotten that in some regions these seem to have continued until quite a late date ; indeed some of the Megalithic tombs and polished stone axes have been dated as late as the third century B.C. A chapter on the peasant potters of Makran, Baluchistan and Sind follows, and this naturally leads on to a discussion of the civilization of the Indus valley. Thanks to Sir John Marshall's work and the excavations at Mohenjo-Daro and other sites, a great deal has come to light of recent years, and this fascinating civilization has become comparatively well known. The period of invasions and the rock paintings and engravings are then dealt with, and in conclusion there are chapters on the 'Dark Age' stone and copper cultures, leading to a chapter which carries on the story to the threshold of history and to the use of iron.

Colonel Gordon has done his job well. It must not be expected that in one small volume the student will find detailed studies of the archæology of the whole of India. But the selections made are judicious and the result does give a connected picture of the past. There are a number of full-page illustrations at the end of the volume and plenty of maps, tables and text figures.

M. C. Burkitt

FLUID SYSTEMS

Chemical Engineering Practice

Edited by Herbert W. Cremer and Trefor Davies. Vol. 6 : Fluid Systems II. Pp. vii + 600 + xx. (London : Butterworths Scientific Publications ; New York : Academic Press, Inc., 1958.) 95*s.* ; 13.30 dollars.

THE latest volume in this series covers a very wide range of chemical engineering operations, although for convenience the editors have labelled the volume "Fluid Systems II". There are fifteen chapters covering gas absorption, fluidization, liquefaction and fractionation of gases, adsorption, leaching, crystallization, colloids, filtration, sublimation and the practice of evaporation. Dr. Norman and his colleagues from Manchester have written two chapters on the principles of gas absorption and the characteristics of packed-column absorption towers. The first chapter is excellent, not only for those in universities and technical colleges but also for all who are concerned with gas absorption. The second chapter, though good, lacks a little of the practical touch one would have liked. The chapter on evaporation practice by Mr. Watkins from King's College, London, assisted by Mr. Macmurray from Scott and Son and Mr. Forker from the Dupont Company, is very readable and covers the usual types of units. More attention might have been given to the actual size of units and some of the practical problems associated with operating evaporators would have been appreciated.

The chapters on fluidization by Dr. Botterell from Birmingham and Mr. Turner from British Petroleum are excellent, and will be looked at very much as indicating the position with this relatively new technique, which offers so much promise of further development. In the same way the chapters by Dr. Gardner of British Oxygen Co., Ltd., and by Mr. Pasteur of J. and E. Hall are welcomed as showing the real problems and successes of low-temperature technology. Low-temperature gas separation is still a new technique but most challenging as a technical process.

Prof. Donald has given an interesting account of leaching, including one or two references to history which are lacking from the other chapters. One is left with the idea that operations of such long standing are not yet carried out with very elegant equipment and there must be room for improvement here. The chapter on the principles of filtration is also written by Prof. Donald.

Dr. Mullin from University College, London, has written the chapters on crystallization, centrifuges, and colloid science. These are all difficult subjects and one would certainly have liked more on the practical difficulties of continuous crystallizers. We cannot learn from these chapters the physical size of units for definite capacities and there are many unresolved problems in the production of true regular crystals.

Mr. Salter, from Dorr-Oliver, and Mr. Hosking, from L. A. Mitchell, have given a clear statement of the variety of filters and the method of selection of equipment. Their section on accessories such as pumps and blowers for vacuum filters is a real attempt to size up these important auxiliaries. One cannot help feeling that some of these units have had their day and are a bit crude ; some pruning of variety might have been suggested by these specialized authors.

This book enables one to see the range of processing problems which are now regarded as the province of the chemical engineer. It is not surprising that in his relatively short history there are many untidy edges to his work. Apart from selecting the right type of unit there is a definite degree of uncertainty as to the ability of the engineer to scale-up such plant satisfactorily.

The book will be welcomed particularly as it provides a discussion of the work in quite a number of fields which have not been adequately covered before in the British literature.

Mr. Cremer has written a foreword to the volume in which he refers to the untimely death of the former managing editor, Mr. Trevor Davies. Mr. S. B. Watkins, head of the Chemical Engineering Department at King's College, London, has taken up the work.

J. M. Coulson

Basic Electricity

(A Course of Training Developed for the United States Navy by Van Valkenburgh, Nooger and Neville, Inc. Adapted to British and Commonwealth Usage by a Special Electronics Training Investigation Team of the Royal Electrical and Mechanical Engineers.) Part 1: Pp. vi+127. Part 2: Pp. vi+121. Part 3: Pp. vi+122. Part 4: Pp. vi+104. Part 5: Pp. vi+117. (New York: The Brolet Press; London: Technical Press, Ltd., 1959.) 12*s.* 6*d.* net per part; 55*s.* net the set.

THIS five-part course, aimed at training technicians rather than electrical engineers, is distinguished by the simple language of its text and its concentration on essentials. It is illustrated to an extent that makes it (or at least the first two parts of it) qualify as a visual aid as well as a text-book. The cartoon-like artistry is a little florid—the sort of thing one might associate with "Jane" but not with "Fighting Ships"; and the going seems slow, by ordinary teaching standards, in the early stages. It soon becomes evident what the authors are up to—using the same technique as the creators of the Li'l Abners and the purveyors of branded goods, to set up an image and attract a loyalty to it; the image being that of the electron. I have no doubt that the early parts would be highly successful in bringing people who would not normally gain a great deal from the printed word to a really sound understanding of the fundamental principles, and simple circuits and meters. The last three parts use the artist in a much more quantitative kind of way. The usual work on alternating current, a.c. circuits, and electrical machinery is done with the minimum of algebra; but every important result is explained and illustrated with the help of vector diagrams and graphs. These parts, in fact, are a very well-conceived text-book of the orthodox type, and contain some new ideas for expounding the more difficult points, which are never shirked. Instructions for experiments are given, with a list of apparatus needed to work through them. The really exacting part of instruction at this level is in making the initial contact with the pupil. The originality and skill that have been lavished on the early stages of the course should ensure for it a very high contact potential. G. R. NOAKES

The Strategy of Chemotherapy

Eighth Symposium of the Society for General Microbiology, held at the Royal Institution, London, April, 1958. Edited by S. T. Cowan and E. Rowatt. Pp. ix+360. (Cambridge: At the University Press, 1958. Published for the Society for General Microbiology.) 35*s.* net.

THIS symposium shows what a complex field of research has developed from Ehrlich's pioneer work on the use of specific substances to attack micro-organisms in the tissues without damage to the host. The organizer invited contributors to suggest fresh methods of attack and the result was a series of papers of extreme diversity in approach, techniques and objectives. They were given by the microbiologist, the pharmacologist, the biochemist and physical chemist, and include such fundamental conceptions as membrane penetration, bacterial cell-wall synthesis and energy-supplying reactions, wherein the research worker is endeavouring to discover some subtle difference in the components of host and parasite which may be exploited to the detriment of the latter. At the other end of the scale are the frankly empirical mass methods used so successfully in the production of the antibiotics and other synthetic drugs, but without any fundamental explanation. These random methods still offer probably the greatest chance for further production of new compounds and therefore have their place in the field of chemotherapy, but the symposium does emphasize the necessity for the combined operations of each type of research worker if chemotherapy is to have a logical basis of development and not be, as one worker defined it, dependent upon intelligent guesswork. H. BERRY

The Native Pinewoods of Scotland

By Prof. H. M. Steven and A. Carlisle. Pp. xvi+368+20 plates. (Edinburgh and London: Oliver and Boyd, Ltd., 1959.) 63*s.* net.

THIS beautifully produced book will be a welcome occupant of the bookshelves of many students of Scottish history and natural history. The subject-matter is both broader and narrower than the title might suggest—broader in so far as the authors discuss much relating to the general history of Scottish forests and to the relationships of pinewoods to woodland of other species, narrower in so far as some features of the pinewoods receive particularly detailed treatment.

The authors trace the history of Scottish woodlands from the Pleistocene period onward through historic times, collating and summarizing an immense amount of evidence from geological, palynological and archæological sources which has never before been brought together. They pass on via a very general ecological account of the pinewoods to a systematic description of all the known surviving examples of woods which are with reasonable certainty composed of naturally regenerated indigenous pine. Carefully prepared maps accompany the descriptions, and show the exact distribution of pine and of other species of trees in the neighbourhood of the pinewoods. This portion of the book is noteworthy for copious historical information which has been gathered together from estate records, early maps, accounts by travellers, etc. An account of Dr. Carlisle's study of the morphological variation of pine in Scotland concludes the book.

A fine series of photographs illustrate the book. I have noticed only one trivial misprint. The book should form a valuable foundation for further ecological work in our western outposts of the European boreal conifer forest, which have so long attracted British naturalists. E. W. JONES

South African Animal Life

Results of the Lund University Expedition in 1950–1951, Vol. 5. Edited by Bertil Hanström, Per Brinck and Gustaf Rudebeck. Pp. 520. (Stockholm: Almqvist and Wiksell, 1958.) 75 Sw. kr.

VOLUME 5 of this series of publications contains accounts on Porifera, Crustacea, Diplopoda, Diptera, Hemiptera and Coleoptera. Six chapters each on the Hemiptera and Coleoptera make up the bulk of this volume. As in earlier volumes the taxonomic treatment is amplified by zoogeographical accounts, and frequently the general accounts are not restricted to the description of the Lund collections, but bring them into relationship with other material. For an assessment of the scope and general merit of this series the reader is referred to an earlier article in this journal (*Nature*, **180**, 56; 1957).

Inside the Living Cell

Some Secrets of Life. By Dr. J. A. V. Butler. Pp. 174+16 plates. (London: George Allen and Unwin, Ltd., 1959.) 21*s*. net.

DR. J. A. V. BUTLER'S former book, "Man is a Microcosm", was reviewed enthusiastically in these pages some years ago. The scope of the present work is much wider, quite apart from the fact that many parts of the subject have advanced radically in the past few years.

The author describes in straightforward language many of the great advances which have been made during the past ten years in our knowledge of the mechanisms which operate within living cells. These include not only the ways in which food materials are taken and transformed into proteins, nucleic acids and other constituents, but also the way in which the ability to make all these is transmitted from generation to generation. In these processes we come very near to the basic mechanisms of life itself. In addition to his excellent account of the normal behaviour of cells the author discusses neoplasms and other abnormalities caused by ionizing radiations, those which seem to occur spontaneously and those which are caused by chemical carcinogens.

Later in the book some abilities of specialized cells, such as those which form muscles and nerves, are dealt with, and an account is given of the immense structures which living cells achieve in the higher animals and finally in man.

Altogether the reader is given some idea of what life has achieved, first, in reaching the level of the cell, and secondly, in elaborating great assemblies of cells in the higher forms of life. Finally, the author discusses the causes and significances of ageing and death, and the meaning of life in the world of atoms.

Throughout, the work is informed by the original work and thought of the author. The book is beautifully produced in every way. The illustrations are particularly good and include photomicrographs such as those by D. A. Sholl of nerve cells in the visual cortex, and by R. W. G. Wyckoff of bacteriophage. The book can be recommended warmly to many classes of reader. Most of it should appeal to the educated adult and it will be invaluable for the general reading of a good science sixth former, or university undergraduate. W. L. Sumner

Organic Syntheses

An Annual publication of Satisfactory Methods for the Preparation of Organic Chemicals, Vol. 37, 1957. Edited by James Cason. Pp. vii + 109. Vol. 38, 1958. Edited by John C. Sheehan. Pp. vii + 120. (New York: John Wiley and Sons, Inc.; London: Chapman and Hall, Ltd.) Each 32*s*. net.

AMONG the 32 compounds for which preparative methods are described in Vol. 37 are benzofurazan oxide, *trans*-2-dodecenoic acid, glutaric acid and glutarimide, norbornylene, parabanic acid, and *ar*-tetrahydro-α-naphthol; and the 31 preparations of Vol. 38 include diphenylacetaldehyde, hendecanedioic acid and several related compounds, monobenzal- and monobromo-pentaerythritol, monovinylacetylene, *trans*-stilbene oxide, and 2-vinylthiophen. Each volume has a cumulative index extending back to Vol. 30. Four enclosed leaflets direct attention to explosions that have been experienced in preparing ethyl azodicarboxylate, methoxyacetylene, and *o*-toluamide, and in storing *p*-tolylsulphonylmethylnitrosamide. John Read

Trends in Birth Rates in the United States since 1870

By Bernard Okun. (The Johns Hopkins University Studies in Historical and Political Science, Series 76, No. 1.) Pp. 203. (Baltimore, Md.: The Johns Hopkins Press; London: Oxford University Press, 1958.) 3.50 dollars; 28*s*.

THIS monograph consists of three essays. The first two discuss the secular trend of the declining birth-rate in the White and Negro population of the United States, respectively. The method used is an analysis of fertility indices (the ratio of children to the total population, and the ratio of children to women of reproductive age) in different States of the U.S.A. The discussion will be of interest mainly to the specialist in demography, and adds little to what is already available in the monograph by Grabill, Kiser and Whelpton, who have surveyed the material in much greater detail. The third essay, however, is of more general interest. Here Dr. Okun surveys the hypotheses and approaches used in explaining birth-rate trends, and attempts a classification and an assessment of the methods that can be used to test the hypotheses. No very definite conclusions emerge, but the essay is a useful summary.

The Structure of Glass

Proceedings of a Conference held at Leningrad, November 23–27, 1953. Translated from the Russian by E. B. Uvarov. Pp. ii+295. (New York: Consultants Bureau, Inc., 1958.) 20 dollars.

THIS translation was sponsored by the Glass Division of the American Ceramic Society and the National Science Foundation with the expressed object of providing a general look at the status of glass science in the U.S.S.R., and admirably does it fulfil its purpose. The fact that this conference was attended by more than 500 delegates from twenty-eight towns of the Soviet Union is itself impressive, and conveys immediately an idea of the large scale on which research in this field is being conducted.

As a report of a conference the volume is excellent: the printed discussion is particularly lively, and occupies 70 pages; 42 papers were communicated to the conference and these account for 228 pages of the volume. Remembering that the conference took place five years ago it would appear that at that time there was no great difference between the topics being discussed in the U.S.S.R. and in Western circles.

It would be easy to dismiss the discussion as being concerned too much with semantics and to criticize some of the ideas put forward. However, examples of similar ideas and arguments are well sprinkled through the literature. The great argument of the conference was on the rival merits of the 'random network' theory of glass structure and the 'crystallite' theory. The proponents of the crystallite theory attacked their opponents on the ground that the randomness was not complete, while their own definition of 'crystallite' was hedged by sufficient qualifications to make it clear that the majority of them did not mean that term to imply anything that could properly be described as a crystal.

Perhaps the fairest summing-up is that here there is realization that the network theory of glass is only a first approximation—a view which is receiving increasing emphasis at the present time.

The translation was well worth while, and all interested in the physics and chemistry of glasses will enjoy reading the book. R. W. Douglas

LIBERTY IN AN AGE OF SCIENCE*

By Sir SOLLY ZUCKERMAN, C.B., F.R.S.
Department of Anatomy, University of Birmingham Medical School, Birmingham

IF, two or three decades ago, one had spoken of science and liberty in the same breath, the emphasis would have been different from my present theme. That period was the era in which the social function of science was a central issue of debate, and it culminated in the almost total mobilization of the scientific forces of our two countries during the Second World War. This War was the turning point. Where previously scientists were seen, according to the interests of the observer, either as dedicated scholars, or as the source of invention, or as the technical guardians of the social services on which an urban civilization depends, to-day they also appear in a number of new guises—as the backbone of national defence ; as pioneers of outer space ; and even as the counsellors of presidents and prime ministers.

The world has come not only to recognize but also to insist that science has a social function ; but, not all the world. There have always been those who have questioned whether the democratic way of life, and a life of liberty, can survive the stresses of rapid economic growth ; and as the hazards of our century mount, their numbers are being reinforced by others who are fearful lest all society becomes a victim of the forces that have been unleashed in our present scientific age. "The scientists think they are God," one exclaims ; "they want to remake the universe ; and we pay the price for their mad ambition."

This is no lonely voice, and it is one that has been heard before. Long before the days of artificial Earth satellites, long before the era of nuclear weapons, George Gissing wrote : "I hate and fear science because of my conviction that for a long time to come, if not for ever, it will be the remorseless enemy of mankind ; . . . I see it bringing a time of vast conflicts, which will pale into insignificance the thousand wars of old and, as likely as not, will overwhelm all the laborious advances of mankind in blood-drenched chaos."

But what science is this that is the enemy of mankind ? Surely not the pure thought or theory which enhances man's understanding ? It is well to consider out of what confusion it is that science presents this ominous look.

The cultivation of science, by which we mean the quest for new natural knowledge through controlled and reproducible observation, can be treated as an endeavour which is either personal and private, or social and public. But however pure or personal may be the object of acquiring a scientific understanding of the universe in which we have our being, science inevitably becomes social or public not only because there can be no awareness of the existence of a new scientific idea until it is communicated from one person to another, but also because pure science frequently turns out to be basic to some practical development—to some piece of applied science—or to some convention of thought, which then starts transforming the environment within which it was distilled. So it is that pure science and applied science have progressed hand-in-hand over the years, the pure fertilizing the applied with ideas, and the applied often providing the pure with the physical apparatus to help in the next intellectual leap forward.

This process has been a major factor in the progressive replacement of superstition by rational theory. And as Condorcet—that great French scientist of the latter half of the eighteenth century who was so powerful a protagonist of human dignity and freedom—wrote : "The progress of the sciences ensures the progress of the art of education which in turn advances that of the sciences"—a reciprocal operation which he did not exaggerate by describing "as one of the most powerful and active causes working for the perfection of mankind".

Man's evolution has also meant the continuous transformation of his social institutions through the directed application of pure scientific knowledge. We talk to-day of living in a new age of science, of a world in the throes of a new scientific revolution : but there is nothing new about this revolution except its speed and its greater hazards. Science has always revolutionized society, ever since some basic discoveries in animal husbandry and crop cultivation made it possible for nomadic life to give way—ten to twenty thousand years ago—to permanent village settlements, and so to the diversification of labour and the beginning of trade.

The transformation of society by scientific discovery and application has continued ever since, sometimes so slowly that decades pass before the historical record reveals much change, sometimes as at present, with ever-mounting force. While it could be argued that the technical advances of the past ten to twenty years transcend those of the rest of human history ; that the speed with which new discoveries are disseminated and applied is now unprecedented ; that the political and economic consequences of all this scientific activity will prove far more profound than those which resulted from past epochs of discovery ; there is nevertheless no immediate reason to suppose that the social process which is involved in to-day's scientific revolution is different in kind from what was entailed in previous phases of rapid change.

If we are to understand the confused position in which the layman and the scientist now stand in relation to each other, we need therefore to examine certain features which characterize the growth of scientific knowledge, and also some which relate to its present impact on social affairs.

What, first, do we mean by the need for academic freedom as it applies to the pure scientist ? One means not only the freedom to investigate those problems which one seeks oneself, but also the fact that significant advances in scientific knowledge cannot be ordered by decree. Every act of creation requires its special freedom. While our theories of

* Substance of the address delivered at the Sixty-fifth Commencement Exercises of the California Institute of Technology on June 12.

thermodynamics, of relativity, or of natural selection, undoubtedly had their antecedent relations, no one could have predicted, before it actually occurred, if, and how, and when any of these major advances in our scientific understanding was to have taken place. Nor would it be possible to force a scientist to make this or that specified discovery. For example, genius though he was, no one could have prevailed upon Charles Darwin, say, in 1830 when he was twenty years old, to anticipate the basic genetic law revealed by Gregor Mendel thirty-five years later. One can employ special measures to encourage this or that branch of science. One can provide the conditions in which pure science flourishes, by multiplying the opportunities which make it possible—the universities, the laboratories, the freedom from other responsibilities. But having done these things, one can only then wait to see what emerges. One cannot in advance specify the shape and content, or determine the possible impact of what is not yet known.

Being unpredictable, it follows that the untrammelled emergence of new scientific ideas is not compatible with any restraint on the liberty of the scientist to roam where his fancy leads. Indeed, once the growth of any set of scientific ideas becomes constrained, it stands in danger of becoming obstructive dogma. A valid scientific hypothesis is never more than the best statement which, for the moment, can be made of the relations of the matters to which it refers, and should be swept away as soon as a better one emerges.

The growth of science thus necessitates freedom, even the freedom to be revolutionary. How then is stability to be achieved in a world in which science has so great an impact? How does science become, as it has often been described, the servant and the handmaiden of freedom?

One's immediate answer is that since economic and military power are to-day proportional to the degree with which scientific knowledge is exploited, science is the defender of the ideal of freedom on which Western democracy rests. In a more particular sense, as many have pointed out before, the applications of science have also provided the apparatus which has made central government powerful.

But surely science is in these respects no more the servant of the democracies than of the authoritarian regimes poised against them, and of the philosophical and political concepts on which they, in turn, are based. In a world of conflicting power, science is both the arsenal and instrument of power—but science *qua* science is always a neutral arsenal and a neutral instrument.

We cannot invest pure scientific knowledge with any inherent moral direction. That is imparted by the way science is used, and we can be certain, therefore, that all sides in the present world struggle will use science and technology in the achievement of their respective national aims; and also in whatever efforts they may make to narrow the ever-widening gap between the developed and under-developed territories of the world.

My first main point, therefore, is that while the growth of fundamental scientific knowledge necessitates complete freedom from restraint, science is not uniquely associated with the preservation of freedom either in the personal or social sphere.

But there is a deeper issue underlying the relation of science and freedom. Let me first define the sense that I propose attaching to the concept of freedom or liberty, which both in isolation, and as the ideal which animates democracy, has always been a major concern of philosophical discussion.

By freedom I mean here the liberty an individual enjoys after the infinite number of degrees of freedom which are open to him in the abstract have been reduced by, say, the give-and-take of social life, still leaving a vast area of choice within which he could either engage in, or desist from, any particular activity. It was essentially in this sense that the great utilitarians of the industrial revolution—Bentham, John Stuart Mill and others who joined them in the battle for justice—conceived of freedom in the ideal society—a society which is governed by common consent for the common good; in which the greatest number enjoy the greatest happiness; in which there is equality of suffrage, and in theory, at least, in educational and economic opportunity; and in which laws and institutions, regulating the behaviour of individuals, are there because the unlimited exercise of one man's liberty would inevitably impose restrictions on that of his fellows.

It is essentially in this social sense, however 'negative' it may be, that liberty is implied in the proposition that science is its handmaiden. Science may, of course, well be the handmaiden of equality in the economic sphere, given, of course, the right political institutions. But is the proposition true in the philosophical sense of the term 'liberty', whether in relation to the concept to which I am directing my observations or to any other idea of liberty which philosophers have examined? Can it be true of the actual environment within which we exercise our freedom—an environment which is not some unreal stratosphere peopled either by abstract shadows of human beings or of social groups? Surely our social environment is a real one which is constantly being transformed by new scientific ideas, and by the application and practical development of these ideas. This transformation constitutes more than a process whereby men are conditioned in their thoughts and actions. Whenever some major development is pursued, for example, the development of machines based on steam, it means that some other path that potentially might have been followed was not followed. A material civilization of motor-cars, of radio, of synthetic fibres, of nuclear power is not necessarily the only form a material civilization might have taken. But now that it has taken that shape, it helps define for us the content and boundaries of the area within which we exercise our freedom.

Liberty, in the sense I am using the term (and I believe to most political philosophers), means the power to act freely within the compass of the institutions which a people may set up in the exercise of their sovereign power, which implies their right to act as they think best as a collective body and which, according to legal theory, "is not restrained in any way except by the limitations inherent in human nature". It is irrelevant here that the exercise of democracy may not infrequently depart from its ideals; or that the institutions which had to be set up to preserve the hard-won freedom of modern times may themselves have eroded the principles they were meant to preserve. The point I wish to make is that science, through its practical impact, is to an increasing extent, almost to a dominant extent, determining the way the presumedly uninhibited sovereign power expresses itself. Because of its achievements in eliminating disease and alleviating pain, through

the food and wealth it has brought, most people to-day prefer to regulate their lives in accordance with scientific discovery rather than in any other way. In that sense they are prepared to constrain their abstract liberties in accordance with what science unfolds, and the riches it brings. Is the choice, we may ask, conscious? Can we know for what it is we are opting? Hobbes, like other philosophers, found liberty consistent with necessity. Is liberty truly consistent with necessity, when necessity is determined by science? Is the sovereign power consciously deciding to develop this or that scientific discovery, and so to determine social development in this or that direction? Or is it merely adapting itself as best it can to what comes out of Pandora's scientific box?

The answer to any of these questions is inevitably bound up both with the constraints and unpredictability of any new major scientific advance. Of course, there are always certain fields of science which are more popular and better supported than others. Scientific knowledge never develops evenly over the whole potential field of knowledge. But in so far as scientific activity is in general confined by past discovery to certain areas, so is our abstract liberty, in effect, constrained. Furthermore, in any field of science, several alternative courses of action might be pursued in search for a solution to a problem. In choosing any one of them, the research worker may deny himself, and others, the opportunity of pursuing another. There is also the increasing complexity of the scientific knowledge which is now being transformed into new remedies, new chemicals, weapons-systems, and so on. The facts which these days transform our lives become more and more difficult to comprehend, and on occasion are still not fully decided when they are applied. If this were not so, would there still be debate—I choose the most urgent example of all—about the hazards associated with radioactive fall-out?

Above all is the fact that the nature and magnitude of potential discovery cannot be defined in advance; any more than can its impact on our social lives. As de Tocqueville wrote: "We entrust ourselves to the future, an enlightened and impartial judge—but one who sits, alas, always too late."

Faraday, Hertz, Curie—what could they have known of the ultimate uses to which their discoveries would be put in the field of electric power, radio and nuclear energy; or of the social and political consequences of their uses. We ourselves, years later, cannot tell what these consequences will be. Can we, to refer to just one more vital question out of many new ones this scientific age is generating, commit ourselves now to more than arbitrary views of the possible political consequences of the elimination of disease and of its complementary change, the explosive growth of population in so many areas of the globe?

Science has created wealth; it has helped in the struggle for freedom from economic exploitation; it has redistributed power. But in doing these things, as it widens the area of material choice, it circumscribes and determines the environment in which we exercise our abstract liberties. That is my second point. Itself demanding freedom, and revolutionary in its ways, science is now determining, in an increasingly unpredictable way, the main issues about which we, as citizens, exercise our freedom of choice. Can there be much more than a fictional verity to the abstract idea that an area exists within which men can enjoy the capacity of unconditioned or untrammelled choice?

Democracy was man's answer to tyranny and exploitation. The only form of exploitation it will never help overcome is the coercion of new knowledge, which, by guiding our social lives into certain channels, limits advance in other directions; the new knowledge which focuses the interests of humanity on goals which cannot be properly charted until they have been achieved. To the philosopher, as I have said, ultimate limitations on the freedom of the individual are set by the inexorable laws of Nature. To the scientist, the limitations are set by the particular laws of Nature man himself discovers, out of a potential infinity of such laws, and from the use to which he puts these laws.

Up to now we have been able to claim that the applications of science have increased the sum total of human happiness. But to-day we stand at a cross-road. The process of applying scientific knowledge is as endless as is the prospect of gathering new knowledge, and the basic scientist is responsible for only the beginning of the cycle of activity which creates a demand for the application of his discoveries. Industrialization has established itself as the one sure cure for poverty in a world the bulk of the population of which still lives by subsistence farming; and history as yet gives no example of any but small communities which have voluntarily turned their backs on higher material standards of living. Instead, a uniformity of desire and demand is generated for the so-called good things of life as the one world discovers how the other lives, and what it itself lacks. Obviously we cannot say that the economic history of the West will be recapitulated as industrialization spreads, and as the chains of the past are broken in distant parts of the world. But we can be all but certain that neither the needy nor the rich will allow the process of applying the fruits of scientific knowledge to stop, either in the national or the international frame. In this process means become ends, because as new ways of doing things are discovered, they transform the things being done, and so their purpose. In these days it is only in theory that one chooses weapons and tactics to achieve a strategy. In fact, weapons often end by determining strategy—and sometimes the purpose behind the strategy.

In my view it is against this force of scientific application that the Gissings of to-day rail—not against science as such; and it is this force which could constrain our democratic liberties, and which, if we ceased being vigilant, could even constrain the liberty of pure and basic science—and by so doing paradoxically destroy itself.

Ideally we think that democracy to-day means government by the representatives of the people by consent of the people. But many to-day also feel that the sovereign power, the people, has through a process of negative democracy, abrogated its rights to a power-*élite*, to a bureaucracy, to what-you-will, which is consciously determining the directions we follow. This, it seems to me, is again too simple. The element of the unknown in government increases with every step we are now taking to apply the fruits of science. If sovereign power is being abrogated, it is less to some governing body, however formed; and more and more to a process of applying scientific knowledge without any real possibility of determining its final consequences. Neither the voice of the majority, nor those through which it is expressed, can proclaim the precise lines of the future.

Where do scientists stand, as ordinary citizens, in this process whereby the application of the fruits of their discoveries can become a potential prison for our abstract liberties? It is argued that because of their special knowledge scientists can be aware of the danger and promise arising from their discoveries, and that therefore they have a special responsibility in relation to the most pressing problems of our time. I should agree with this, if it meant no more than that scientists are better able to appreciate the scientific facts. For how can the scientist as such, who is not responsible for its application, accept the responsibility for predicting some vast social transformation that might result from what seems an innocent observation at the time it is made?

But I should agree all the more if one coupled with this view of the scientist's responsibility the thought that in the problem of preserving our liberties lies the most important reason for regarding an education in science as constituting to-day an essential part of an education in the humanities. For if an understanding of social and political purpose is one of the aims of the liberal arts, then that aim cannot be realized until their scope is widened to embrace a proper understanding of the scientific knowledge the application of which is now so rapidly transforming our intellectual and material environment.

Science, technology and humanism seem to have assumed that order of importance in the determination of our affairs. I do not know how it is in the United States; but over the post-war years the changes which the tacit application of science and technology have occasioned in Great Britain seem far more profound than any that have been brought about through the overt discussion of social values or social goals. If this kind of thing is happening, can the humanities continue as a potent educational discipline without encompassing an understanding of the social forces which derive from the application of the natural sciences? Scientific literacy, we are told in a recently issued report on education, will need to be far more widespread than it is "if we are to solve the problems of this age". Undoubtedly this is needed, but alone it is not a sufficient condition to ensure the solution of our problems—for here I agree with Aldous Huxley that "higher education is not necessarily a guarantee of higher virtue or higher political wisdom". What we most need to learn is that in the major scientific matters which now affect human destiny, one cannot safely take decisions for to-day unless we realize that those same decisions determine the future. This realization may not lead to the right decisions; but it might help obviate some of the worse.

SATELLITE OBSERVATIONS OF SOLAR COSMIC RAYS

By PAMELA ROTHWELL and CARL McILWAIN
State University of Iowa, Iowa City

On three occasions during August 1958, large increases in the intensity of charged particles outside the Van Allen radiation zones were detected by the *Explorer IV* satellite 1958 epsilon, at high magnetic latitudes and rather low satellite altitudes (270–650 km.), where the Geiger tubes carried in the satellite normally count only cosmic rays. Figs. 1, 2 and 3 show that the charged particle intensity in both counters increased sharply with magnetic latitude, above about 60°, on August 16–17, August 23–24 and August 26–27. (We have defined 'magnetic latitude', λ_{dip} from the magnetic dip angle δ at the point of observation, through the dipole relation $2 \tan \lambda_{dip} = \tan \delta$.) Different symbols have been used for each satellite pass on any one day, recorded at the microlock station in Van Buren, Maine, in the geographical longitude range (95° W.–45° W.). The time-interval for each pass (usually about 5 min. duration) is given, and each point has been characterized by the altitude in kilometres at which the observation was made. The charged particle detectors in the satellite have been described in detail elsewhere by Van Allen *et al.*[1]. The two Geiger counters (one shielded with 1·6 gm./cm.² lead, and the other unshielded except by the satellite hull) could detect protons of energies greater than 40 MeV. and 30 MeV., respectively, and electrons of energies greater than about 5 MeV. and 3 MeV. The omnidirectional geometric factors ranged from 0·140 cm.² to 0·823 cm.² in the shielded counter, and from 0·140 cm.² to 0·705 cm.² in the unshielded counter. Table 1 gives the upper and lower limits to the omnidirectional fluxes of particles which would produce the highest observed counting rates in (*a*) the unshielded counter

Table 1

Date August 1958	Time of satellite pass (C.T.)	(*a*) Flux through unshielded Geiger counter (particles/cm.²/sec.)	(*b*) Flux through shielded counter (particles/cm.²/sec.)	(*c*) Ratio of counting rates unshielded/ shielded	(*d*) $E_{min.}$ (MeV.)	(*e*) $E_{max.}$ (MeV.)	(*f*) Elapsed time after 3 + solar flares (hr.)
16	11·17–11·19	$86 > J_{\gamma u} > 17$	$78 > J_{\gamma s} > 13$	$1·1 \pm 0·3$	~ 90	~ 200	6·8
16	13·11–13·15	$193 > J_{\gamma u} > 38$	$179 > J_{\gamma s} > 30$	$1·1 \pm 0·2$	~ 60	~ 200	8·7
17	11·01–11·06	$240 > J_{\gamma u} > 48$	$86 > J_{\gamma s} > 14$	$2·8 \pm 0·3$	~ 90	~ 200	30·5
17	12·56–13·00	$121 > J_{\gamma u} > 24$	$43 > J_{\gamma s} > 7$	$2·8 \pm 0·5$	~ 60	~ 200	32·4
23	09·22–09·30	$577 > J_{\gamma u} > 115$	$193 > J_{\gamma s} > 33$	$3·0 \pm 0·2$	~ 90	~ 250	19·1
23	11·14–11·23	$445 > J_{\gamma u} > 88$	$150 > J_{\gamma s} > 25$	$2·9 \pm 0·2$	~ 35	~ 250	21·0
24	10·59–11·05	$140 > J_{\gamma u} > 28$	$37 > J_{\gamma s} > 6$	$3·8 \pm 0·5$	~ 35	~ 250	43·8
26	08·26–08·34	$1{,}010 > J_{\gamma u} > 200$	$465 > J_{\gamma s} > 79$	$2·2 \pm 0·1$	~ 85	~ 350	8·4
26	10·22–10·28	$1{,}300 > J_{\gamma u} > 265$	$515 > J_{\gamma s} > 88$	$2·5 \pm 0·1$	~ 55	~ 350	10·3
27	08·06–08·15	$143 > J_{\gamma u} > 28$	$46 > J_{\gamma s} > 7$	$3·1 \pm 0·5$	~ 85	—	32·0
27	10·04–10·08	$132 > J_{\gamma u} > 26$	$50 > J_{\gamma s} > 8$	$2·6 \pm 0·5$	~ 55	~ 350	34·0

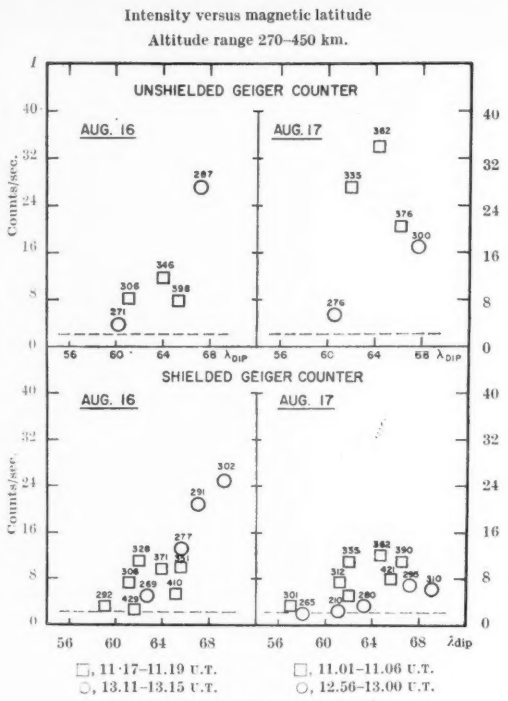

Fig. 1

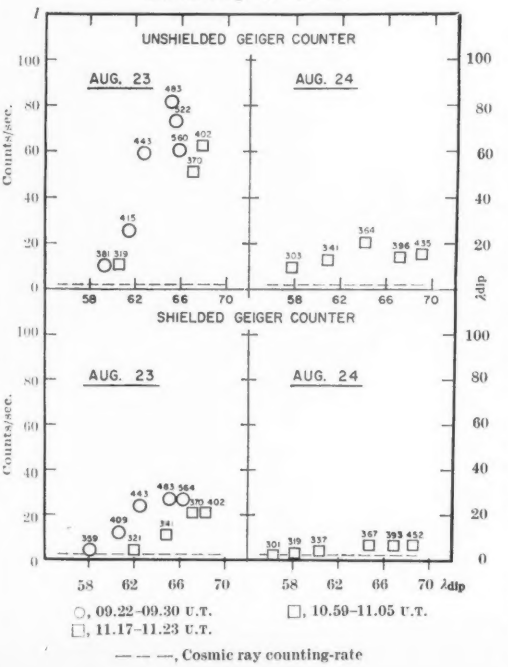

Fig. 2

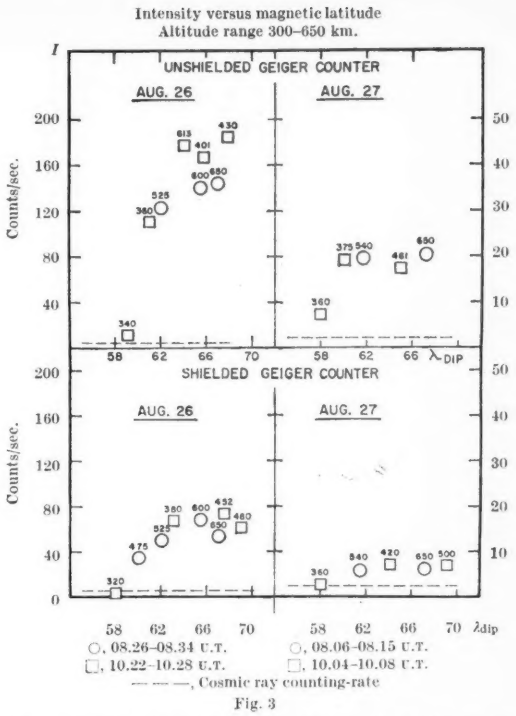

Fig. 3

(J_{0u}), (*b*) the shielded counter (J_{0s}), and (*c*) the ratio of these counting rates (unshielded/shielded) at each satellite pass on which an increase in intensity was observed. The cut-off energies for protons, at (*d*) the highest magnetic latitude on each pass ($E_{\min.}$) and (*e*) the lowest latitude at which counting rates in excess of the cosmic ray rate were recorded ($E_{\max.}$), are estimated from the local values of the Earth's magnetic field[2].

The particle fluxes are at least one or two orders of magnitude greater than the normal cosmic ray flux. It seems unlikely that these intensity increases are due to soft particles from the outer Van Allen radiation zone, because :

(*a*) *Explorer IV* cuts through the outer zone (as observed with the Geiger counters) at about 56° magnetic latitude, that is, farther south than the intensity increases reported here.

(*b*) The ratio of counting rates between the unshielded and shielded Geiger counters in the outer zone is typically, about 30 or 40 to one, in contrast to the comparable counting rates observed in both counters at the higher latitudes.

The ratios unshielded/shielded are reasonably consistent with the hypothesis that the charged particles are protons the energies of which lie between $E_{\min.}$ and $E_{\max.}$ The wide limits placed on the estimated fluxes are due to the uncertainty in the absolute geometric factor for the counters in the proton energy-range 30–100 MeV.

We suggest that the intensity increases are in fact due to solar protons, associated with the large solar flares which occurred at 0432 U.T. on August 16, 1417 U.T. on August 22, and 0005 U.T. on August 26[3]. Strong support for this suggestion is provided by measurements made from balloons and with riometers during this period.

(1) Anderson[4] and Winckler *et al.*[5] measured an increase in charged particle intensity at balloon altitudes above Churchill, Canada (magnetic latitude 77°), and Fairbanks, Alaska (magnetic latitude 64°), on August 22 and 23, and have identified the particles as solar protons of energies up to a few hundred MeV. It is almost certain that the satellite has recorded the same event. (The increased intensity was not observed until August 23 because there was no pass over Van Buren after 1100 U.T. on August 22.) Anderson *et al.*[6] deduce a differential number energy spectrum $n(E)\mathrm{d}E = K(t)E^{(-5\pm0\cdot2)}\mathrm{d}E$ (where t is the elapsed time after the solar flare) for the solar protons in the energy-range 100–400 MeV. At 1115 U.T. on August 23 they estimate that the flux of particles with energies greater than 100 MeV. was about 1·5/cm.²/sec. Intensities observed from the satellite at that time suggest that a spectrum of this form may well extend down to about 30 MeV.

(2) Leinbach and Reid[7] have suggested recently that the absorption of cosmic radio noise, measured with riometers following large solar flares, is due to ionization of the upper atmosphere by solar protons. H. Leinbach (private communication) and Hultquist and Ortner[8] have observed three such events, commencing August 16, August 22 and August 26, in the riometers at Thule (Greenland), Fairbanks (Alaska) and Kiruna (Sweden). Absorption effects of this type occurred on twelve other occasions, between July 1, 1957, and September 30, 1958 (H. Leinbach, private communication).

During the period August 16–27 no increase in intensity was observed in the Canadian cosmic-ray neutron monitors at Resolute, Churchill, Sulphur Mountain and Deep River[9] at magnetic latitudes of 88°, 77°, 61° and 62°, respectively, but it is not surprising that protons with a steep number-energy spectrum and maximum energies of a few hundred MeV. produced no detectable effects near sea-level.

The ratio of the maximum counting rates in the two counters increased significantly during each event. This suggests that either: (*a*) the shape of the energy spectrum of the solar protons changes, and relatively more low-energy particles arrive at later times; or (*b*) that some particles with energies below the usual magnetic cut-off energy can arrive at a given location later in the event.

Freier *et al.*[10] have, in fact, reported that protons with energies below the usual measured cut-off were found at balloon altitudes over Minnesota on March 26, 1958, three days after a large solar flare, and at the time of a magnetic storm. When the Earth's field is disturbed, some charged particles can probably be admitted to regions normally 'forbidden' to them, and particles with energies below the normal cut-off may arrive at a given latitude during, and perhaps for some time after, the disturbance. During the period August 16–27 'sudden commencements' occurred at 0622 August 17, 0228 August 22, 0140 August 24, and 0303 August 27[11]. The lowest ratios unshielded/shielded occurred on August 16 before this period of magnetic activity.

There is now evidence from several sources which strongly suggests that solar protons with energies up to a few hundred MeV. quite frequently bombard the upper atmosphere at high latitudes for some days following a large solar flare. The five widely observed, extraordinary increases in cosmic-ray intensity near sea-level which have occurred during the past twenty years of continuous observation are probably unusually energetic examples of a common solar phenomenon, namely, the acceleration and ejection of protons with energies approaching those of galactic cosmic-ray particles.

We should like to thank Prof. J. A. Van Allen and Dr. K. A. Anderson for many interesting discussions. This work has been assisted by the U.S. International Geophysical Year project 32.1 of the National Academy of Sciences, the U.S. Army Ordnance Department, the Office of Naval Research, and the Atomic Energy Commission.

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A BORE-HOLE TO THE EARTH'S MANTLE: AMSOC'S MOHOLE

By GORDON LILL and WILLARD BASCOM

AMSOC Committee, National Academy of Sciences—National Research Council, Washington, D.C.

MAN'S knowledge of the interior of the Earth has been largely obtained by indirect methods, and although a great deal is now known about the qualities that subterranean materials must possess, numerous uncertainties remain. There is now a project under way, sponsored by the AMSOC Committee of the U.S. National Academy of Sciences to obtain corroborative evidence about the nature of the interior of the Earth by the direct method of drilling a hole completely through the oceanic crust to obtain samples of the mantle. Since the boundary between the crust and mantle is known as the 'Moho' (after Prof. A. Mohorovičić of Yugoslavia, who first described the seismic discontinuity there) it seemed reasonable to contract the project name to 'Mohole'.

The American Miscellaneous Society, founded in 1952 as a whimsical reproof of scientific societies which are sometimes too specific for their own good, uses its cable address, AMSOC, in the alphabetical world of Washington. It has no formal members, officers, by-laws or publications; and there is a bent towards geophysics.

On the subject of drilling through the crust of the Earth, however, the AMSOC group has been formally

organized so that it can receive funds from the U.S. National Science Foundation. The original members of the Committee were: Gordon Lill (chairman), Prof. Maurice Ewing, Dr. William Heroy, Prof. Harry Hess, Dr. Harry Ladd, Dr. Arthur Maxwell, Prof. Walter Munk, Prof. Roger Revelle, Dr. William Rubey, Dr. Joshua Tracey and Willard Bascom (technical director).

The Mohole project in more or less its present form was born at a breakfast at Prof. Munk's house in California, at which he led the conversation on the need for a geophysical analogue for the space exploration programme. The suggestion of Dr. Frank Eastabrook, made in *Science* (October 1956) for the digging of a "Geophysical research shaft", had set forth the principal scientific advantages of direct sampling. But AMSOC, unaware at the time of that suggestion, proposed a deep drilling project.

The following September, in Toronto, at the meeting of the International Union of Geodesy and Geophysics, a resolution was passed "urging the nations of the world to study the feasibility and cost of an attempt to drill to the Mohorovičić discontinuity at a place where it approaches the surface". A hole 10–15 km. deep on an oceanic island was suggested. The sponsors were Harry Hess, Roger Revelle and T. F. Gaskell.

The question of the structure and material of the interior of the Earth is a puzzle which has long challenged the mind of man. In all major aspects the most acceptable present hypothesis holds together very well. This is remarkable, for it requires that there be reasonable agreement between at least eight sub-sciences, all of which make indirect measurements. Studies of astronomy, meteorites, volcanoes, geological structure, gravity, seismic waves, the magnetic field, and heat flow each contribute to the total knowledge.

If one assumes that meteorites are the wreckage of a planet similar to the Earth and that the rocks spewed out by volcanoes (the seismic precursors of which begin well below the Mohorovičić discontinuity) contain samples of mantle material, then we already have samples of the deep rocks. Moreover, Harry Hess believes that mantle rock actually outcrops (at St. Paul's Rocks in the mid-Atlantic, in Japan and in California). Astronomical observations give the total mass, the average density and the moment of inertia of the Earth.

But in the main, evidence about the interior of the Earth has come from earthquake waves. By the combination of tedious computation and great skill, seismologists have worked out characteristics of the planet which keep within the limits set by the other evidence.

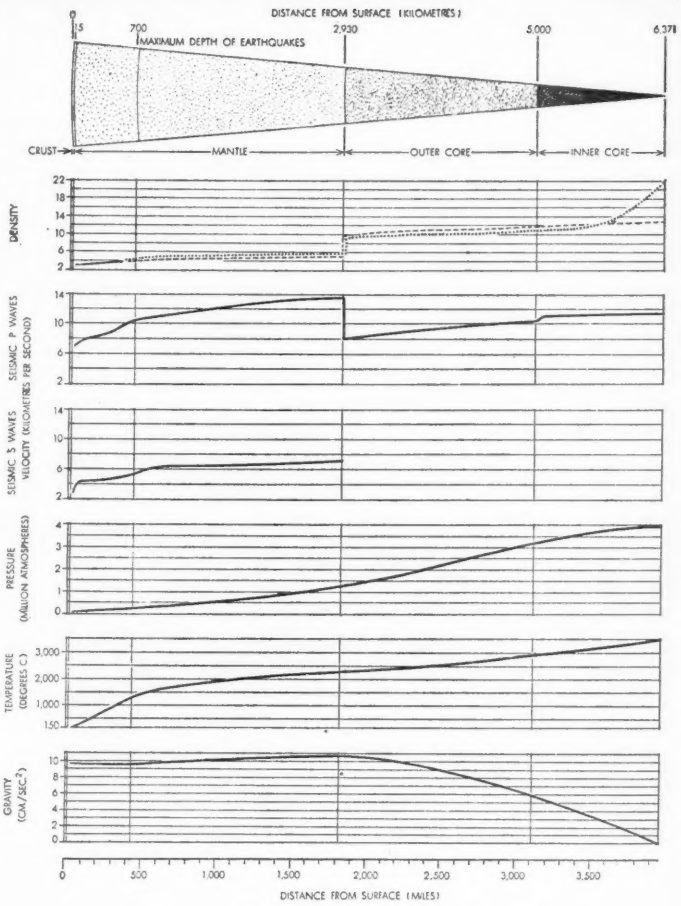

Fig. 1. The interior of the Earth

The hypothesis of inner and outer cores surrounded by a thick mantle and capped with a thin crust has stood the tests of many years; now the problem is to refine the information and to obtain evidence which cannot come from further advances in seismology. The composition of the mantle, which represents about 85 per cent of the volume of the Earth, is the principal problem of geophysics to-day, for although a lot is known about it, uncertainties remain (Fig. 1).

The exact mineralogical and rock composition, the density, strength, temperature, the amount of radioactivity, the thermal and electrical conductivity—all these will contribute immeasurably to the understanding of the Earth and its origin. Moreover, they will serve to enhance the value of the indirect geophysical measurements. Finally, some new and entirely unexpected piece of evidence may be unearthed that will cause science to revise substantially its concept of the Earth.

The crust is closer and easier to study than the interior, but even so it is more controversial. Generally it is agreed that continents represent relatively thick blocks of andesitic rocks, and that ocean basins are composed of much thinner basaltic rocks—the average thicknesses being about 30 km.

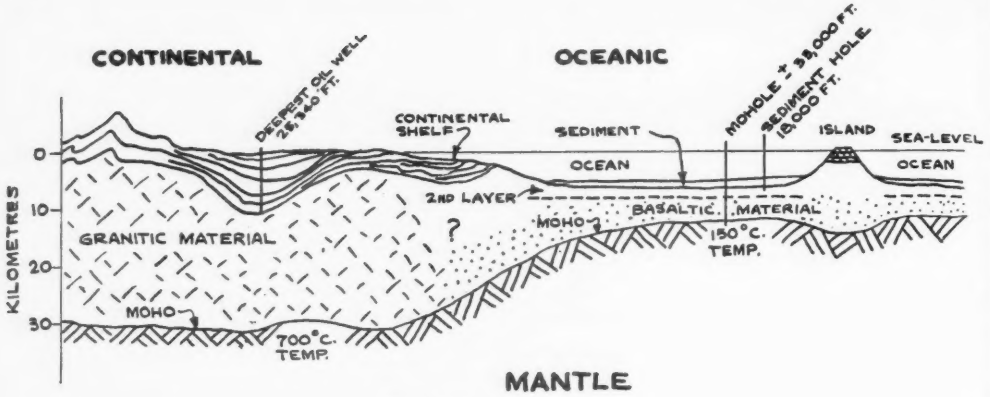

Fig. 2. The crust of the Earth

and 10 km. respectively. The crust seems to act as though it is floating on viscous plastic mantle material; however, the response time is long, and certain anomalous areas not in isostatic equilibrium complicate the problem. The Moho, which defines the boundary between crust and mantle, is recognized by an abrupt increase in the velocity of seismic waves—from about 7·0 km./sec. to 8·2 km./sec.

As the Earth developed, the water which reached its surface naturally ran downhill and covered the lower, thinner basaltic material, forming an ocean.

The composition of the oceanic crust is studied by sea-going seismologists who use pairs of ships—one setting off explosions, the other listening. In this way it has been discovered that beneath much of the ocean there are three main layers of material: (1) the soft sediments, (2) the 'second layer', and (3) the 'third layer' (Fig. 2).

The soft sediments of the deep sea floor (red clays and calcareous oozes) have been repeatedly sampled with corers which have penetrated as much as 20 m. into the bottom and reached as far back as Cretaceous time.

The seismic evidence suggests that the sediments are remarkably uniform in thickness, averaging about 0·4 km. Unfortunately, this is much too thin to agree with the figure one gets by multiplying present sedimentation-rates by the supposed age of the oceans. So one very large question to be answered is: What happened to the rest of the sediments? Moreover, it seems possible that the record of early evolution, missing on land, could be preserved in the lowest sediments.

There are at least four theories about the composition of the 'second layer'—all of which begin with the knowledge that it conducts seismic waves at 4·5–5·5 km./sec. It may be compacted sediments, basalt, dolomite or softer sediments screened by a layer of basalt; usually it is 1 or 2 km. thick.

The 'third layer' has a seismic velocity of about 6·5 km./sec.; it is commonly called basalt but, as Hess points out, this is more a matter of 150 years of tradition than of evidence. In fact, some scientists doubt that there are as many as three layers; others think there are more.

One of the interfaces (possibly the Mohorovičić discontinuity) may represent the primordial surface of the Earth. It may have a surface something like the face of the Moon to-day; it may be covered by a layer of meteoritic material or perhaps a conglomerate. It may give evidence of our early atmosphere and ocean, or it may have been altered beyond recognition. These speculations have served to make the proposed exploratory holes even more exciting.

Many of these suggestions have been discussed and debated in the literature. Harry Hess believes that the Mohorovičić discontinuity represents a frozen isotherm; J. F. Lovering thinks it represents a temperature–pressure relationship which has caused a phase change from an ecologite mantle to a basalt crust. Tuzo Wilson believes that continental andesitic material must be rising from the mantle—from greater depths than the basalts. He notes that K. Sapper's figure of 0·8 km.³/year over geological time would account for the volume of the continents, and that a slightly higher rate of volcanism in the early stages would allow for the emission of an oceanic crust as well. Sir Harold Jeffreys believes that the ocean crust is too rigid to permit sideways motion of the continents, but recently there has been renewed interest in Wegener's continental drift theory. There are points of disagreement on the distribution of radioactivity, on the interpretations of seismic velocities, and on the causes of oceanic trenches.

The very fact that there is not agreement is a good reason for some direct exploration (if there were no controversy there might be even greater suspicion that something was wrong).

Some of these questions will be resolved if a continuous core of the various layers beneath the sea-floor can be brought into the laboratory for study and analysis. In addition, in the hole from which the core is taken measurements can be made of temperature, heat-flow, the magnetic field, plastic deformation and seismic velocity.

It is therefore the objective of the AMSOC Committee to see that a continuous, oriented core to the mantle is obtained and that the hole(s) are thoroughly instrumented. Some of the instruments already exist; others will have to be developed or miniaturized to fit in the hole (which will be about 6 in. in diameter at the bottom). No geologist or geophysicist doubts the value of such determinations; the question is: How can it be done, and for how much money?

In *Nature* of September 13, 1958, Dr. Gaskell examined some of the technical problems of deep-hole drilling. However, as the AMSOC feasibility study progresses, new objectives have been developed and

Table 1. Reach of Drill required to achieve Various Objectives

	Phase	Pacific						Atlantic	
		Clipperton Island area 10° 53′ N. 105° 09′ W.		Guadalupe Island area 28° 45′ N. 117° 31′ W.		Due south of San Diego, Cal. 5° 47′ N. 123° 59′ W.		North of Puerto Rico 20° 40′ N. 66° 30′ W.	
		km.	ft.	km.	ft.	km.	ft.	km.	ft.
Depth of water		3·1	10,100	3·5	10,700	4·3	14,000	5·5	18,000
Depth to bottom of sediment	I	3·3	10,400	3·6	10,900	4·8	15,700	6·0	19,600
Depth to bottom of second layer		4·2	13,800	5·2	17,000	5·5	18,000	8·0	26,200
Depth to Mohorovičić discontinuity	II	8·6	28,100	10·8	35,500	9·7	31,800	9·6	31,500

Note. Geophysicists think in kilometres, but drillers work in feet.
Pacific data from R. W. Raitt, Scripps Institution of Oceanography.
Atlantic data from J. Worzel, G. Sutton *et al.*, Lamont Geological Observatory.

new drilling technology has been disclosed so that now Gaskell's views need to be revised. For example, the idea of drilling from an oceanic island has been abandoned because recent studies indicate that the mantle is as deep as 17 km. under the islands that have been studied. Developments in floating drilling platforms make it appear that deep-water drilling is feasible in any event; besides, we need the sedimentary results. A review of the temperature situation suggests that temperatures in the mantle beneath the ocean crust will be less than 200° C. At several sites where seismic work has been done, the total reach of the drill stem from the surface of the water to the mantle will need to be only 30,000 ft. Thus as the project develops, the objectives seem more attainable with less difficulty and expense.

Table 1 shows the length of drilling pipe required to reach the surface of the various layers beneath the sea-floor at four sites which are under consideration.

Inspection of these figures shows that a drill reaching to 6 km. (20,000 ft.) will give results on the upper three layers. Beneath that it is another 3–5 km. to the Mohorovičić discontinuity. For this reason the project will be divided into two phases. The first of these involves the modification of existing equipment for drilling holes in the upper layers. The second phase—which will take us on to the Mohorovičić discontinuity—will probably require a completely new engineering design, for the total length of the drill pipe must be well over a mile beyond that used in the deepest oil well to date (25,340 ft. hole by Phillips Petroleum in western Texas).

The objectives of the first phase would be to obtain the best possible samples of the upper layers while testing out deep-water drilling methods. For example, no one is sure how closely a ship must be held in position in deep water while it drills, but several schemes have been proposed which would probably keep it within a circle the diameter of which is less than 3 per cent of the depth (12,000 ft. or so of water). The forces due to the drag of ocean currents on the drill pipe and casing are as yet unknown because of the lack of reliable deep-current data. Questions of how often casing will have to be run and how it will be supported, of how well the soft sediments can be cored and if sea water is a satisfactory drilling fluid will be answered by the first test holes.

There are four floating platforms which mount intermediate-depth oil rigs drilling in shallow water off the coast of the United States. Many of the problems of ocean drilling have been ingeniously solved by these operators, so that only minor modifications of standard drilling techniques are needed. Several ways have been found for re-entering the hole and re-circulating drilling muds; these require that a riser pipe, conductor or casing reach to the surface. It is even possible to abandon a hole temporarily and recover it again.

In depths of 35–360 ft., holes have been drilled to nearly 12,000 ft. *CUSS I*, for example, now drilling for oil off the California coast, is a well-designed vessel that would make an excellent deep-drilling experimental platform if it were equipped with a heavier draw-works or hoist (such as are available on the open market) and a deep mooring system.

Holding a ship in position in water two and a half miles deep might be accomplished by (1) anchors which are explosion-jetted into the bottom and connected to the ship by neutrally buoyant hawse lines of synthetic material; (2) a dynamic anchoring system in which a group of outboard propulsion units (which can exert propulsive force in any direction) are centrally controlled by an operator who holds his position by watching taut-line buoys and/or listening to a vertical beam of underwater sound rising from a transducer fixed to the bottom.

Thus, the mooring, drilling, setting of casing and riser pipe, coring and instrumentation all appear to be well within the bounds of our technology. Engineering work has started and funds are being solicited.

As the feasibility study progresses, the original cost estimates have shrunk and it now appears that the entire project might be carried out for about 15 million dollars. This is not an inconsiderable sum, but it is much less than that of a rocket-propelled moon-probe, the ostensible objective of which is to learn about the nature and origin of the solar system. It seems a little foolish to go off to look at the Moon when we do not know what lies a few kilometres beneath us on our own planet.

The first phase of the drilling can be accomplished for about 2·5 million dollars; the second for about 9·5 million dollars. It is hoped that the project will be financed jointly by private interests and by the U.S. National Science Foundation. Certain related aspects of oceanography and of doing heavy work at sea might be supported by the U.S. Navy, although no direct military application is foreseen.

When drilling will start is uncertain; it will depend on the length of time needed to complete preliminary work and to obtain funds. Work could begin on the test holes before the end of 1959. The scientific planning of objectives, locations and instruments; the collection of necessary data and the re-survey of the most promising areas are already under way.

AMSOC believes that this series of holes which will eventually sample the mantle of the Earth is likely to produce the greatest advances in man's knowledge of the Earth in our time.

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ASYMMETRICAL DELIVERY IN RABBITS

By Dr. LUIZ MACEDO COSTA* and Dr. ARPAD CSAPO

The Rockefeller Institute, New York, 21

THE experiments of Corner and Allen[1] and Allen and Reynolds[2], performed on rabbits, promised an understanding of the mechanism by which pregnancy is maintained and terminated in mammals. They also provided us with a key substance which controls these processes, the ovarian steroid progesterone.

The thirty years which followed these discoveries, however, brought disappointments. The different consequences in different species of ovariectomy or oxytocin infusion upon pregnancy; the lack of correlation between uterine activity and the concentration of progestational compounds in body fluids; and the lack of success in predicting effective progesterone therapy in women led many investigators to believe that either progestational compounds do not have a key role in the control of the pregnant uterus, or else a variety of mechanisms operate in different species.

These conclusions are challenged by a striking experiment of Nature which strongly implies that the maintenance of pregnancy is more a local than a systemic affair, thus allowing an explanation of the differences cited above. When a woman who has a duplex or bicornate uterus bears twins, one in each horn, the infants may be born several weeks apart, showing that in the same woman at the same instant conditions can be appropriate for the maintenance, as well as for the termination, of pregnancy[3].

Classical endocrinology limits our thinking to a systemic hormonal control of the uterus by which the glandular product is distributed uniformly in the target organs. This simple experiment of Nature, however, suggests to us that such a systemic control may not operate in all instances. A 'local' effect may be considered instead, when the organ of secretion and its target are in direct contact, allowing diffusion of an active compound from one cell to the next. Thus the local effect of placental progesterone has been postulated and described[4] as an alternate mechanism.

The existence of such a local mechanism could explain present controversial issues concerning the mechanism of the maintenance of pregnancy. Species differences could be looked upon not as differences in basic principles, but, for example, as differences in timing and in magnitude of the shift from ovarian (systemic) to placental (local) progesterone effect; or

* Grantee of the Rockefeller Foundation. Present address: Department of Physiology, University of Bahia, Salvador, Brazil.

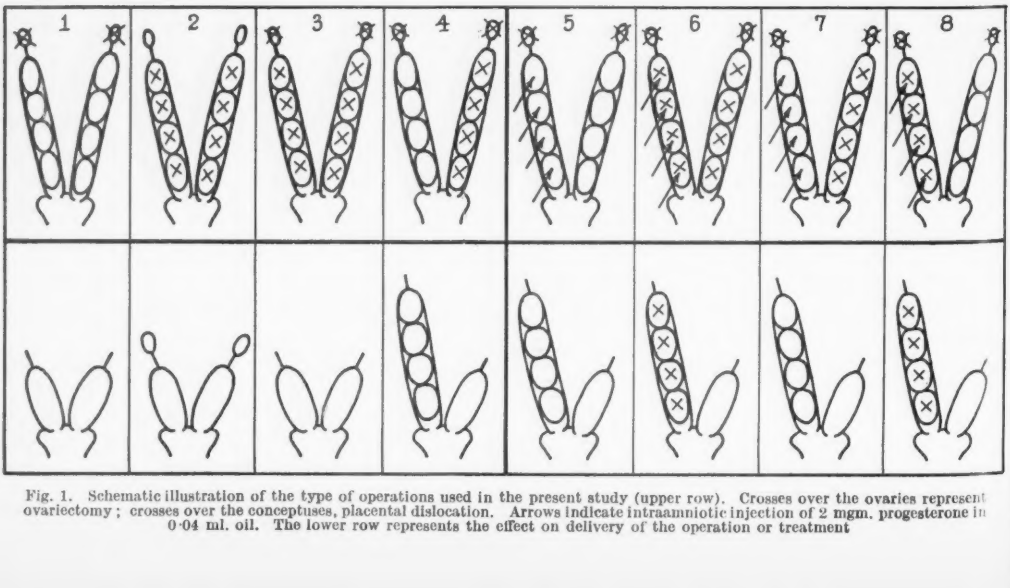

Fig. 1. Schematic illustration of the type of operations used in the present study (upper row). Crosses over the ovaries represent ovariectomy; crosses over the conceptuses, placental dislocation. Arrows indicate intraamniotic injection of 2 mgm. progesterone in 0·04 ml. oil. The lower row represents the effect on delivery of the operation or treatment

Fig. 2. Asymmetrical delivery in rabbits, induced on the twenty-fifth day of pregnancy. The numbers on the left represent the type of operation as illustrated schematically in Fig. 1. The first picture on the left is taken immediately after the operation; the second is made on repeated laparotomy after delivery is completed in one horn, and the third after the undelivered horn is opened and the fœtuses and placentas examined

as differences in the metabolism and elimination of progesterone, dependent on the exposure of progestational compounds to the systemic circulation, prior to their uptake by target organs. The concentration of progestational compounds and their changes in concentration in body fluids would not be expected to reflect quantitatively the endocrine condition of the uterus because much higher concentrations than occur in the blood or in the urine could be present in key positions at the myometrial cell; in fact, body fluids may contain only the 'leakage' of a local arrangement or what is left from destructive and eliminating processes. The lack of conclusive evidence for the effective use of progesterone in therapy would become a challenge rather than disappointment, because an effective local supply of placental progesterone could be therapeutically initiated only by a similar local application, or by forms of progesterone not subject to systemic destruction.

To demonstrate a local effect of placental progesterone on the myometrium, we studied thirty-five pregnant rabbits in the present experiments. It is generally believed that pregnancy in rabbits is entirely maintained by ovarian progesterone, not supported by placental contribution. We suspected, however, that even in rabbits there may be progesterone production, or effective metabolism, in the placenta in late pregnancy[4a,b,d]. In women, on the other hand, during the last six months of pregnancy the placenta seems to substitute completely for the endocrine function of the ovaries[5].

In our colony of New Zealand white rabbits labour can be induced with 1 I.U. 'Pitocin' (Parke-Davis), intramuscularly, in 94 per cent of the animals 31 days after mating. Only 7 per cent of the animals deliver after similar treatment (even if repeatedly applied), if the animal is less than 30 days pregnant.

We ovariectomized rabbits bilaterally (op. No. 1) on the twenty-fifth day of gestation (duration of pregnancy = 32 days) and found that 13 hr. after the operation 1 I.U. of 'Pitocin' successfully induced delivery.

If the ovaries were not removed (op. No. 2), but all the placentas in both uterine horns were dislocated (by gently pressing the uterine horn at the placental implantation site), placental function ceased and delivery was successfully induced by 'Pitocin' 20 hr. later. This is evidence that the rabbit placenta is indispensable for the maintenance of pregnancy.

If the two procedures, ovariectomy and placental dislocation, are combined (op. No. 3), labour can be induced 9 hr. later. These observations suggest that in the rabbit both the ovaries and the placentas contribute to the maintenance of pregnancy. When both these possible sources of progestational compounds are removed, the myometrium has enough stored material to defend pregnancy for 9 hr. against the labour-inducing effect of 1 I.U. 'Pitocin'. The placentas can prolong this period for four additional hours and the ovaries for 11 hr. This suggests that the ovarian contribution is three times as great as the placental.

If after any of these operations 'Pitocin' is not administered, spontaneous delivery ultimately occurs; but the time between operation and delivery, as well as the time needed for delivery, is greatly prolonged. Also, the mother may destroy or partly eat the

uterine contents, which makes accurate timing and observations difficult. For this reason we induced labour with 'Pitocin'.

It may be argued that the rabbit placenta only stores, but does not produce, an active progestational compound. The following experiment, however, suggests that the placental contribution is not only storage, but also synthesis or effective metabolism. If ovariectomy is combined with the dislocation of one set of placentas, in one horn only (op. No. 4), this horn alone delivers 9 hr. later on 'Pitocin' administration, whereas pregnancy is maintained in the other horn. This asymmetrical delivery, resulting from the presence of a set of functional and another set of non-functional placentas in two horns, respectively, is indication of the production of an active compound as well as evidence of the local effect of the placenta.

It might be said, however, that the active compound of the placenta is not like progesterone, but is an entirely different compound. This is unlikely, since the local effect of the dislocated placentas can be substituted for by the injection of 1–2 mgm. progesterone into the amniotic sac. If only one horn is treated with progesterone in the ovariectomized animal, delivery is always asymmetrical. The untreated horn delivers first, irrespective of whether the placentas in one horn are dislocated or not (op. Nos. 5–8). The time when delivery occurs reflects a functional or non-functional set of placentas, but the phenomenon is the same, that is, delivery is asymmetrical if the distribution of progesterone is asymmetrical. Whether the litter is alive or not does not alter the picture, nor does the mechanical irritation of the uterine horn during the operation.

These observations are best explained as follows. Pregnancy in rabbits is maintained by a joint contribution of an active progestational compound by the ovaries (systemic) and placentas (local). The placental contribution is less than that of the ovaries; but both organs are needed to maintain an effective concentration of the active compound in the myometrial cell. When the defence is effective, labour cannot be induced by 'Pitocin'; if it becomes ineffective, labour can be induced. When the systemic effect of the ovaries is suspended by ovariectomy the local effect of the placenta controls the uterus and if this local effect is asymmetrical, labour is asymmetrical.

In women, an early and complete shift from ovarian to placental hormone production could result in a dominant local progesterone effect early in pregnancy. This would lead to an 'endocrine asymmetry', resulting in asymmetrical function. Such an asymmetry is exaggerated in a bicornate uterus when endocrine function in one placenta fails earlier than in the other. Functional asymmetry of the human uterus offers attractive explanations of puzzling problems concerning normal and abnormal pregnancy and delivery.

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WARREN SPRING LABORATORY, STEVENAGE

IN setting up Warren Spring Laboratory at Stevenage "to carry out process research and development over a wide field not limited to particular areas of technology", the Research Council for the Department of Scientific and Industrial Research expressed its conviction that, when necessary, the Department's research stations should change in function and objective to meet the needs of changing situations. The Council considered that the Fuel Research Station had largely fulfilled the aims in view when it was set up, and that current needs were satisfactorily catered for by researches going on elsewhere; it decided, therefore, to close down the Fuel Research Station, and to transfer the staff to a new Laboratory in Stevenage, with new programmes. To ensure that there should be no likelihood of an impression being gained that the Fuel Research Station was being continued at Stevenage, or that the title of the new Laboratory might appear to restrict the field of activity, it is named after a lane which used to run across the site.

Of the work carried out at the Fuel Research Station only two programmes have been transferred to the new Station, namely, research on the abatement of atmospheric pollution, and on the synthesis of oils and chemicals by the Fischer–Tropsch process.

There had been a number of substantial indications of need for research in the field of mineral processing, and it was decided that this should form one of the new projects to be undertaken; there had also been indications of need for work on a pilot scale in various fields which the Department had not been able to meet. With these pointers, it was decided to build a laboratory in a modern industrial style, to be as flexible as possible, to house in the first place a staff about the size of that of the Fuel Research Station, and with facilities for both laboratory research and pilot-scale work.

The main three-story laboratory building is 372 ft. long and 37 ft. 6 in. wide (Fig. 1). It is based on a 4-ft. module, which is expressed elevationally by vertical posts supporting floors and roof, and by internal posts centrally along the length. The main spine corridor is set to one side of the central supports. The only solid internal walls are those of the corridor and the secondary staircases; all other partitioning is of light, demountable, prefabricated construction, which can be placed in any desired position between the outer walls and the inner corridor walls, subject only to the basic 4-ft. module.

Gas, water, electricity, compressed air are available at every third module (12 ft.) along a perimeter distribution system.

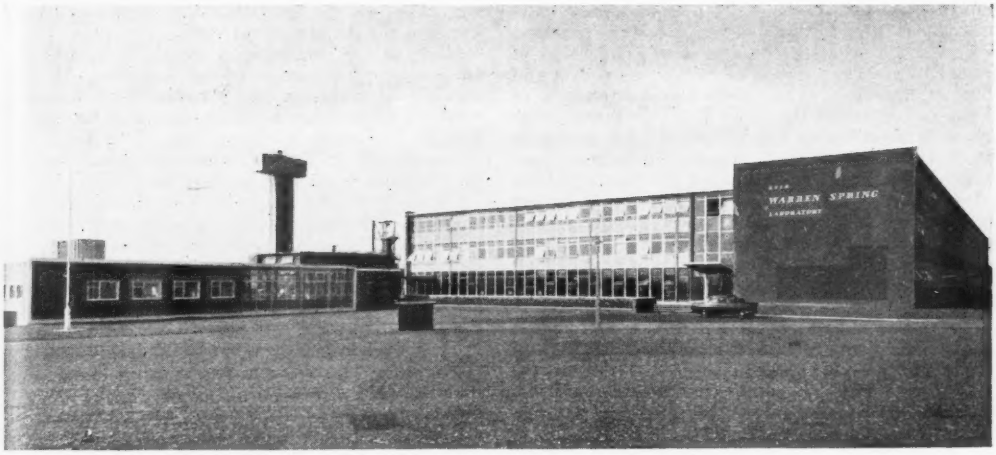

Fig. 1. The Warren Spring Laboratory, Department of Scientific and Industrial Research

The building is heated by panel-type radiators; made-up dummy panels matching them are inserted between the radiators to give the appearance of a continuous radiator panel along each wall between the concrete columns at 12-ft. centres. The radiators and the dummy panels conceal the services which run around the perimeter of the building. The dummy panels can be readily removed when service connexions are required. Fume cupboards are ranged along the inner, corridor walls, each cupboard having its own extract duct which discharges at roof-level.

The finishes are simple, self-coloured, fair-faced brickwork being used throughout, except in laboratories with special functions. With the exception of laboratories which are adapted for wet processes, floor finishes are in linoleum.

A three-story administration block runs at right angles to the main laboratory building; it is similar in construction and design except that there is a lower ceiling height.

There are three pilot-scale buildings, each 90 ft. long by 55 ft. wide by 37 ft. 6 in. maximum height. In two of them, a 20-ft. wide section is 20 ft. high only. These buildings are linked to the main laboratory block by a corridor with small-scale laboratory units on each side. The buildings have folding doors to the side bays to permit the introduction of heavy plant at any point. The structure is carried by precast concrete posts. Vertical cladding, above a brick protective walling, consists of asbestos–cement sheeting and patent glazing; the roofs are of asbestos–cement decking overlaid with bituminous felt.

The workshops and engineering stores occupy a large steel-framed building comprising six east-light bays, each 60 ft. by 30 ft. minimum headroom.

Since steam is required night and day for process purposes, two fully automatic, oil-fired, high-efficiency boilers are used, with a nominal pressure of 120 lb./sq. in.; one is rated at 10,000 lb. and one at 5,000 lb. of steam per hour. The front of the boiler house is fully glazed with a patent system permitting ready removal in sections when boiler tube replacements are necessary, so that it is possible to reduce the dimensions from front to rear. A high-level water reservoir, in reinforced concrete, has been designed integrally with the boiler flue (see Fig. 1).

Service mains run in open, splay-sided trenches to avoid the expense of underground ducts or the unsightliness of overhead gantries.

The total cost of the establishment, including buildings, services fixed, laboratory fittings, library bookshelves, and all site works was approximately £620,000.

Research Programmes

Atmospheric pollution. Purely by coincidence the closing of the Fuel Research Station occurred simultaneously with the introduction of the Clean Air Act; it was therefore particularly apposite to review the programme in starting at the new station. The work now being undertaken follows naturally from that begun at the Fuel Research Station, and is designed to meet the requirements of the Ministry of Housing and Local Government.

The principles of smoke-elimination that have proved successful in reducing smoke from hand-fired boilers on land are being applied to marine boilers. The possibility of developing after-burners to burn smoke in various situations is being investigated.

The properties of smokes from different sources are being examined with special reference to the constituents that might be injurious to health. The occurrence of oxides of nitrogen in the atmosphere under different conditions is being studied.

In the new investigations of air pollution there is a need for greater accuracy than has been possible in some of the measurements made in the past. As a matter of urgency a review is being made of the principal instruments at present in use; this work is being undertaken by the Scottish Branch of the Laboratory at Thorntonhall.

Micro-surveys are in progress to examine the concentration of various types of pollution at different types of site in a limited area. The results of such investigations will be important, for example, in helping to determine the value of smoke-control areas, and in assisting those responsible for deciding the height of siting of large industrial chimneys.

Process development. Synthesis of oils and chemicals from carbon monoxide and hydrogen is being studied as part of a project to develop, if possible, an econ-

omic process for producing oil from coal. The development of oils from coal is a two-stage process: the first stage involves the complete gasification of the coal to yield a mixture of carbon monoxide and hydrogen, and the second the catalytic conversion of the gas mixture into the desired end-products. The work at Warren Spring Laboratory is concerned only with the second of these stages. Economic considerations indicate that the most promising version of the Fischer–Tropsch process for use under British conditions is the slurry process, in which the gas mixture is passed through a suspension of powdered catalyst in molten wax at temperatures of 250–300° C., and at pressures between 5 and 30 atmospheres.

The objectives of the programme are: (1) to develop an iron catalyst of longer life and higher activity than those at present available and one that will yield a high proportion of desired end-products; (2) to select operating conditions (gas composition, temperature, pressure) to combine a high reaction velocity with a given distribution of end-products; (3) to obtain data necessary to design a full-scale reaction vessel.

Synthesis gas is produced on the site at a rate of 4,500 std. cu. ft. per hr. in a standard, water-gas generator operated by the Engineering Services Division. There are arrangements for feeding carbon dioxide with the steam so as to vary the hydrogen: carbon monoxide ratio between 1·15 and 0·6. The gas is purified from hydrogen sulphide in Gastechnik towers and washed with caustic soda to control the carbon dioxide content. It is then compressed to 15 atmospheres pressure in the first two stages of a four-stage compressor, passed through the active carbon scrubbers to remove organic sulphur compounds, and then further compressed in the third and fourth stages to a pressure of 120 atmospheres.

The study of catalysis, which has been proceeding over a number of years at the Fuel Research Station, has brought to the team concerned considerable experience which should prove of value in some of the new programmes which it is hoped to undertake in the future.

Mineral processing research and development. Dr. M. G. Fleming, of the Bessemer Laboratory of the Royal School of Mines, has been appointed consultant to this Division.

It seems probable that for some time a fair proportion of the effort of this Division will be engaged on sponsored work on particular ores; but it is hoped that basic investigations will include: (1) a study of grinding in the presence of additives such as surface-active agents; (2) the kinetics of bubble attachments to mineral surfaces, as a contribution to the knowledge in the field of froth flotation; and (3) a study of the behaviour of mineral particles in a high-tension field, and the modification of this behaviour by various surface treatments.

The laboratories are equipped to handle most laboratory-scale mineral-dressing operations such as flotation, jigging, tabling, heavy-media separation, wet and dry magnetic separation, and high-voltage separation. In the hydrometallurgical field, facilities are available for atmospheric and pressure leaching, for fluidized-bed roasting, chlorine metallurgy, and solvent extraction. Pilot-plant facilities enable primary crushing operations to be carried out on a scale up to 2½ tons per hour, and flotation plant is available for treating up to 1,000 lb. per hr. It is possible to carry out full-scale tests with radioactive tracers. The Division has a Mineralogical Section, but relies on the Physical and Chemical Services Division for its analytical work.

Many of the problems on which work is likely to be necessary concern overseas deposits. Already a number of requests for investigations have been received from overseas territories, and an Overseas Mineral Processing Advisory Committee has been set up to advise on the selection and priorities of the programmes of interest to these territories.

Chemical engineering. It will be apparent that chemical engineering must play a large part in practically all the major activities of the Laboratory, and the decision of the Research Council to transfer "the work on Chemical Engineering . . . carried out at the National Chemical Laboratory to Warren Spring Laboratory" will readily be understood.

The Division has three functions: (1) to carry out research on physical operations which play an important part both in processes which are under development in the Laboratory, and those in more general use in industry; (2) to undertake research in the field of chemical engineering sponsored by industry or by Government departments; (3) as a result of these functions to accumulate basic information in chemical engineering for use by other sections of the Laboratory and industry.

Bearing in mind work that is already going on elsewhere in the Department on heat transfer and on fluid flow, it is proposed in the first instance to concentrate on the field of mass-transfer, and in particular to obtain results which will permit more accurate prediction of the performance of gas–liquid contacting equipment, and thus to facilitate the design of distillation columns, gas-absorption towers, and reactors of the liquid-phase type, of which the Fischer–Tropsch slurry reactor is a particular example.

Four main lines of study are being followed, namely, bubble dynamics, gas-liquid mass transfer rates, fluid mixing, and specific problems in gas absorption with chemical reaction.

The National Engineering Laboratory of the Department has sponsored work at Queen Mary College, London, on the synthesis of organic compounds for use as drop-wise condensation promoters and has evaluated their effectiveness. The proposed work at the Warren Spring Laboratory is being planned in consultation with the National Engineering Laboratory and is intended as a study of the mode of action of these promoters in order to facilitate the development of compounds which will be effective for prolonged periods with a wide range of metal surfaces. It is proposed to study the mechanism of attachment of synthetic promoters to metal surfaces by methods of radiochemical labelling and to observe the subsequent history of these substances under conditions of use in heat exchangers.

Physical and Chemical Services Division. This provides a comprehensive central service in the fields of analysis, both by chemical and physical methods, instrument development, physical measurement, and photography. Special equipment includes gas chromatography, quartz and infra-red spectrometers, and equipment for X-ray diffraction and fluorescence spectrometry.

Engineering Services. This Division has a drawing office which undertakes design of pilot-scale plant for the Laboratory; it has an industrial staff of approximately 120, and well-equipped workshops.

Intelligence. In addition to the library and editorial services which are essential to any research estab-

lishment, the Intelligence Division is setting out to provide an information and project appraisal service. A start has been made, for example, in building up a centre of information in mineral processing, by assembling data from a wide variety of sources in such a way that they can be used in research and industry.

From what has been described it will be apparent that there is a wide choice of field before Warren Spring Laboratory, and that at the moment the main problem is that of selection, and of allocation of priorities. In addition to the factors which govern the work of other laboratories of the Department of Scientific and Industrial Research, there is the task of undertaking sponsored work to a greater extent, and on a larger scale. Such work may be carried out for Government departments or for industry, and it may be on a fully confidential basis. The special facilities of the Laboratory will also be available for use, in certain circumstances, by teams from industry, which can work in collaboration with the research staff of the Laboratory.

The programme is regularly considered by a Steering Committee, appointed by the Research Council, the present members of which are: Sir Harry Jephcott (chairman), Sir Harry Melville, Dr. R. Holroyd, Mr. D. A. Oliver and Mr. S. H. Clarke.

OBITUARIES

Mr. T. L. Eckersley, F.R.S.

THE death of T. L. Eckersley on February 15 removed another of the rapidly dwindling band of pioneers in the field of radio research, among whom he was notable both for his theoretical and practical work. His interest in electromagnetic waves was aroused while he was still at school at Bedales; but it was during the First World War, after studying at University College, London, and Trinity College, Cambridge, with some years at the National Physical Laboratory in between, that he made his first big contributions to radio-wave propagation. These were his explanation of 'night-effect' in direction-finding observed in Egypt and Salonika, in which he invoked the existence of an upper ionized layer giving rise to a reflected wave with variable polarization characteristics, and his observation of coastal refraction which he sought to account for in terms of the properties of Zenneck surface waves.

He was thus among the first to obtain evidence of the presence of the ionosphere by the reflexion of radio waves and so began a life-long interest in the magneto-ionic theory of propagation. His first work, however, on joining the Marconi Co. after the War was a classical research into the properties of earth screens for increasing the radiation efficiency of long-wave aerials, followed by his analysis of the results of observations made on very long-wave transmitters by K. W. Tremellen and C. M. Allnutt during a round-the-world expedition. For more than twenty years Tremellen was Eckersley's personal assistant, and his patient observational work formed the basis of the succession of papers which Eckersley wrote on short-wave radio transmission.

The last of these was on scattering from 'clouds' in the ionosphere, a subject which has since become of great practical importance in the development of the ionospheric 'forward scatter' communication system. Not only did all this work lay the foundation of much of our knowledge of the part played by the ionosphere in long-distance propagation, but it also led to many advances in technique, for example, in the field of accurate direction-finding and in the measurement of field-strength and polarization characteristics.

Although he would not have claimed to be a pure mathematician, he had a consummate ability to apply mathematics to physical problems. Indeed, many of his experimental researches were preceded or supported by elegant analysis. He had a great interest in modern physics, especially in its quantum and relativistic aspects, and it was the knowledge so acquired that inspired some of his finest work in radio. It was the phase integral treatment of potential barriers in atomic theory that led him to his brilliant applications to ionospheric and ground-wave propagation, while in the scattering of α-particles he found an analogy for the scattering of radio waves as a function of wave-length, cloud size and scattering angle.

Eckersley had something of the absent-mindedness associated with genius, which was reflected in the style of his writing and made some of his papers difficult for others to read. He was thus not as well known in the world at large as he deserved to be; but in due course full recognition among scientists came with his election to fellowship of the Royal Society in 1938 and the award of the Faraday Medal of the Institution of Electrical Engineers in 1951. He was also a well-known figure at international radio conferences, especially at the C.C.I.R. and U.R.S.I. assemblies.

He was proud of the fact that he was a grandson of T. H. Huxley, and he was most happy in his family life, his wife being Eva, the daughter of Barry Pain, the Victorian novelist, who survives him with a son and two daughters. She is an able pianist and composer, and their home at Danbury, Essex, was often visited by distinguished musical friends. He was a delightful host, for he combined great courtesy with a delicate sense of humour, and though he did not play himself he had a great love of music.

At the time he died he had become almost completely helpless from multiple sclerosis, the first symptoms of which had appeared more than twenty years ago. In spite of increasing disability, he remained at work throughout the Second World War as scientific adviser to the Inter-Services Ionosphere Bureau at the Marconi Research Laboratories, and after his retirement in 1946 he continued to work at home for several more years.

During this period he published a number of papers, his devoted wife acting as his amanuensis. There is no doubt that it was her amazing courage and cheerfulness that maintained his life for so long, and indeed it was to pneumonia during the influenza epidemic that he finally succumbed. The loving care which surrounded him during those last years was a source of inspiration to all who witnessed it.

G. MILLINGTON

Prof. A. O. R. Windaus

On June 9 it was reported from Göttingen that Adolf Windaus had died in his eighty-third year. He had retired as professor and director of the University Chemical Laboratory at Göttingen in 1938, and was made emeritus professor and director in 1944.

Windaus was born in Berlin in 1876, educated at the Universities of Berlin and Freiburg-im-Bresgau and became *Privatdozent* in 1903. After a short period at Innsbruck, he was elected to Göttingen in 1915. He was awarded the Nobel Prize for Chemistry in 1928, and also received the Baeyer, Pasteur and Goethe Medals.

To those interested in steroids, Windaus's name will stand with that of the late Heinrich Wieland as the greatest in the period of German pre-eminence in discovery about the chemistry and physiology of these substances. Most of his publications between 1903 and 1928 were about cholesterol and described, *inter alia*, the preparation of complexes with digitonin, solanin, etc. (1909, 1918), the nature of the side-chain (1913) and the relationship to coprosterol (1916) and to the bile acids (1919). Papers also appeared on stigmasterol (1906, 1924), sitosterol (1918, 1924), hydrodeoxycholic acid (1923, 1926), chenodeoxycholic acid (1924, 1925, 1926) and on 'β'-phocæcholic acid (1928). All this work and much more, including some on heart poisons and saponins, was done without modern knowledge of steroid formulæ; yet Windaus's fundamental discoveries stand largely unchallenged to-day. His work on scymnol (with W. Bergmann and G. König, *Hoppe Seyl. Z.*, **189**, 148; 1930) was the first on the chemistry of this substance. The paper with Alfred Hess, of Columbia University, New York, entitled "Sterine und antirachitisches Vitamin" and published at the session of the Gesellschaft der Wissenschaften zu Göttingen on January 28, 1927, clearly recognized that both ergosterol and an impurity separable from cholesterol acquired antirachitic activity on irradiation with ultra-violet light. Parallel work had already begun in England (for example, I. M. Heilbron, E. D. Kamm and R. A. Morton; O. Rosenheim and T. A. Webster; *Chem. and Indust.*, **45**, 932; 1926); it was energetically pursued there, and also by Windaus and his colleagues until, in 1931, success in isolating a pure vitamin D was announced almost simultaneously from Göttingen and Hampstead, London. From irradiated ergosterol, F. A. Askew, H. M. Bruce, R. K. Callow, J. St. L. Philpot and T. A. Webster (*Nature*, **128**, 758; 1931) obtained calciferol, and Windaus and O. Linsert (*Liebigs Ann.*, **489**, 269; 1931) vitamin D_2: these substances were later found to be identical, although the separate names were retained.

'Vitamin D_1', originally reported as pure by the German workers (*Liebigs Ann.*, **489**, 252; 1931), was later proved (*ibid.*, **493**, 259; 1932) to be a molecular compound of vitamin D_2 and lumisterol.

For Windaus, this was by no means the end of the vitamin D problem. Doubts as to the identity of calciferol (vitamin D_2) and the antirachitic vitamin of fish-liver oils persisted, and C. E. Bills (*Physiol. Rev.*, **15**, 1; 1935) summarized evidence that the antirachitic vitamin in irradiated (impure) cholesterol and in cod liver oil (as measured in 'rat units') is more potent for chicks than the vitamin (calciferol) in irradiated ergosterlly.

Windaus brilliantly recalled that J. Mauthner and W. Suida in 1896 (*Mh. Chem.*, **17**, 579) had oxidized cholesterol with chromic acid to 7-ketocholesterol, and, with H. Lettré and Fr. Schenck (*Liebigs Ann.*, **520**, 98; 1935), he reported the conversion of this substance into 7-dehydrocholesterol. Irradiation of this gave a mixture from which was isolated (Windaus, Fr. Schenck and F. von Werder: *Hoppe Seyl. Z.*, **241**, 100; 1936) vitamin D_3, identical with the natural vitamin obtained from tunny liver oil by H. Brockmann (*Hoppe Seyl. Z.*, **241**, 104; 1936) at Göttingen. Windaus's later papers were about the chemical nature of natural forms of vitamin D and the chemistry of irradiation products of ergosterol and 7-dehydrocholesterol.

Windaus's publications, which ceased in 1944, remain as an inspiring example of what a great intellect can still accomplish in scientific discovery.

G. A. D. Haslewood

Dr. F. Busemann

Dr. Felix Busemann, who died on April 30 at the untimely age of fifty-one, was an outstanding authority in his chosen subject, electrical transmission, as is his brother, Adolf Busemann, one of the leading German aerodynamicists now in America. Trained at the Institute of Technology, Darmstadt, he became later assistant to the professor of electrical machine design there, and in 1934 joined the firm of Siemens Schuckert in Berlin, becoming one of a team concerned with future developments in electrical transmission. This team had as one of its assignments that of high-voltage direct-current transmission. Starting with a pilot scheme between Charlottenburg and Moabit, it followed by planning the Siemens Schuckert half of the major Elbe–Berlin project. After the Second World War, Dr. Busemann was chosen by the Darwin Panel and came to Britain in 1946 to report on the German work in this field.

Busemann found the social climate in Britain so akin to his temperament that he shortly accepted an offer to join the staff of the Electrical Research Association and continue his studies on d.c. transmission. These resulted in a masterly series of fourteen reports covering all aspects of the subject with the exception of valves, for the study of which facilities were lacking. He played a major part in the planning of a pilot scheme which, had it matured, would have placed Great Britain in the van of development. He was without doubt the foremost authority on high-voltage direct-current transmission in Britain, and his loss will be greatly felt.

With the temporary cessation of interest in direct-current transmission, Busemann turned his versatile mind to other aspects of transmission. Among these he devised, jointly with W. Casson, a classic programme of full-scale experiments on power-system stability (Cliff Quay), described in a paper before the Institution of Electrical Engineers last year. More recently, he had been concerned with mechanical and thermal properties of soil and utilization of power cables. To all these he brought quick appreciation of decisive factors and great facility in analysis and exposition.

Behind a natural modesty Busemann had great personal charm and humour as well as perception. He was a musician of almost professional attainment and gave much service to his church and the social activities of the Electrical Research Association. He will be remembered by all who knew him for a long time to come. He leaves a widow and two daughters.

L. Gosland

Miss Grace M. Sickles

GRACE M. SICKLES, associate research scientist in the Division of Laboratories and Research of the New York State Department of Health, died on June 29 at Troy, New York. An eminent bacteriologist and virologist, Miss Sickles had been a member of the Health Department since 1918, with a two-year period of service (1919–20) in the Communicable Disease Laboratories of the United States Army. She was a graduate of the New York State College for Teachers and a member of the principal scientific societies in her fields of research.

Miss Sickles was associated with Dr. Augustus B. Wadsworth in an extensive series of investigations on the production and standardization of anti-pneumococcus, antimeningococcus and antistreptococcus sera, studying, as early as 1938, the action of immune serum in conjunction with chemotherapy in experimental streptococcus infections. Some of Miss Sickles's studies of diphtheria toxin and on the antibiotic activity of micro-organisms from the soil were carried out at the Marine Biological Laboratory, Woods Hole, Massachusetts.

Miss Sickles was the discoverer with Dr. Gilbert Dalldorf in 1947 of the coxsackie virus. The virus was identified during a study of outbreaks of poliomyelitis in New York State. It was named after the village in which the first two recognized human infections occurred. The coxsackie group now includes more than a dozen viruses which are common sources of infection in man.

Mr. W. E. Perry

THE sudden death on June 5 of Mr. W. E. Perry, a senior principal scientific officer at the National Physical Laboratory, Teddington, removes one of the leading figures in the field of radioactive and radiation standardization. Born in 1903, Perry took his degree from Nottingham and joined the Laboratory in 1928. He was responsible for re-measurement of the National Radium Standards in 1934, and for the subsequent development of radioisotope measurements. Later, as head of the Radiology Section at the Laboratory, he had charge of the work on radioisotopes, X-ray dosimetry, neutron standardization and radiocarbon dating; and had an international reputation for his scientific integrity and wide knowledge in these subjects. At the time of his death, he was preparing material for the ninth International Congress on Radiology at Munich, in his capacity as chairman of Committee I of the International Commission on Radiological Units and Measurements.

NEWS and VIEWS

The British Association : New President

SIR GEORGE THOMSON, master of Corpus Christi College, Cambridge, has been elected president for 1960 of the British Association for the Advancement of Science, in succession to Sir James Gray. Sir George has had a distinguished career as a physicist, as a man who gave outstanding service to the Atomic Energy Project in its early days and as master of Corpus Christi College. The son of the late Sir J. J. Thomson, he was educated at Trinity College, Cambridge, obtaining a first-class degree both in the Mathematical and in the Natural Sciences Tripos. After service in France with the Army, followed by research on aeronautical problems, he was appointed to the chair of physics at Aberdeen in 1922, where he carried out the epoch-making work on the defraction of electron beams by thin metal foils, thereby establishing beyond doubt the wave nature of the electron. For this work he was awarded the Nobel Prize for Physics in 1937. Between 1930 and 1952 he was professor of physics in the Imperial College of Science and Technology, London, and was chairman of the first British Committee on Atomic Energy, the Maud Committee, appointed in 1940. He has played a considerable part in the development of the subject ever since, being interested not less in its social as well as in its scientific aspects. Since his appointment to the mastership of Corpus Christi College, his interest in physics has continued and he has published work on gas discharges and has been chairman of Section *A* (Mathematics and Physics) of the British Association. Both on account of the great distinction of his scientific work and his interest in the wider implications of scientific advance he will be a most welcome president of the British Association.

Director of the Royal Aircraft Establishment : Prof. M. J. Lighthill, F.R.S.

PROF. M. J. LIGHTHILL, Beyer professor of applied mathematics at the University of Manchester since 1950, has been appointed director of the Royal Aircraft Establishment, Farnborough, in succession to Sir George Gardner, who is succeeding Air Chief Marshal Sir Claude Pelly as controller of aircraft at the Ministry of Supply in October.

Prof. Lighthill has made outstanding contributions in many fields of fluid dynamics as well as in more general spheres of pure and applied mathematics. His applications of the fundamentals of mathematics to various aeronautical problems have been significant and widespread. He is particularly well known for his theoretical work on jet noise; this work, which has been largely substantiated by experiment, relates the noise to the turbulence in the jet. He has always displayed a continuing interest in the practical application of his theories, and has been for a number of years a member of the Aeronautical Research Council. Prof. Lighthill was educated at Winchester and Cambridge, and was elected to the fellowship of the Royal Society in 1953 at the early age of twenty-nine.

Royal College of Science and Technology, Glasgow : Sir David Anderson

SIR DAVID ANDERSON, who is to retire from the post of director of the Royal College of Science and Technology in December 1959, was appointed principal of Derby Technical College in 1926 at the age of 31. In 1930, he became principal of the Central Technical College, Birmingham, and in a period of 16 years which spanned the arduous war years, he laid the foundations of the College of

Advanced Technology, designated as such by the Minister of Education in 1956. In this period, too, he became increasingly concerned with the problems of technical education at national level. This was especially true of his work as a member of the Percy Committee which reported in 1946, and greatly influenced the development of post-war technical education. He was president of the Association of Principals of Technical Institutions in 1932, and chairman of Council of Association of Technical Institutions in 1951. He was a member of Council of the Institution of Mechanical Engineers during 1941–42, 1948–50. First and foremost a Glasgow man, he was educated at Whitehill School, then at the then Royal Technical College, and served his apprenticeship with the North British Locomotive Company. He returned to the College as director in 1946, and the new engineering block, the recently opened students union, the Residential School of Management Studies at Bearsden, and the new students residences are visible signs of his vigorous leadership. He has continued to serve on a large number of bodies at national level, and was knighted in 1957. After the manner of present times, we may hope that Sir David will not retire from all public work, otherwise the constructive contributions of his incisive mind will be greatly missed.

Dr. S. C. Curran, F.R.S.

The Governors of the Royal College of Science and Technology, Glasgow, have announced the appointment of Dr. S. C. Curran as principal in succession to Sir David Anderson, the retiring director. Dr. Curran studied at the Universities of Glasgow and Cambridge, graduating M.A., B.Sc., Ph.D. (Glas.), and Ph.D. (Cantab.). His early researches were concerned with radiation phenomena and new methods of detection. While at St. John's College, Cambridge, and the Cavendish Laboratory, he pioneered in investigations of proton capture.

During the Second World War he shared in the successful work of the Royal Aircraft Establishment on proximity fuses and of the Telecommunications Research Establishment on the research and development of centimetre radar, having charge of one of the groups responsible for H_2S and ASV; thereafter he joined the British Mission on Atomic Weapons in the United States. At Berkeley he discovered the original form of the scintillation counter and the vacuum carbon arc. Later at the University of Glasgow he introduced the modern form of proportional counter, determining with it the form of novel beta-spectra such as that of tritium. An active research group soon grew up under his leadership.

In early 1955 he joined the Atomic Weapons Research Establishment, where he later became a chief scientist and member of the Management Board responsible for the divisions of Nuclear Research and Electronics. He also served as visiting member on the Harwell Management Board. A considerable growth of nuclear research has taken place at Aldermaston during his years there.

Dr. Curran was awarded the D.Sc. and Kelvin Prize of Glasgow in 1950 and elected to fellowship of the Royal Society in 1953.

Jean Senebier (1742–1809)

Jean Senebier, who died of "une cruelle maladie" at Geneva 150 years ago on July 22, 1809, is an anomalous figure in the history of botany. A clergyman untrained in the scientific method, yet possessing the true scientific spirit, endowed with curiosity, intelligence, and industry, he had many interests: theology, botany, microscopy, physics, chemistry, meteorology, library classification. His tiresome rhetoric prevented his being appreciated by his generation. The son of a protestant tradesman of French origin, he was born on May 6, 1742, at Geneva, where he became pastor in 1765 and chief librarian in 1773. In 1792 political unrest banished him from the city for seven years. Senebier is remembered chiefly for his studies on the influence of light on vegetation. Jan Ingenhousz, an engineer of Dutch extraction, in 1779, introduced the concept of balance of animal and vegetable life by showing that plants generate dephlogisticated air. This activity was demonstrated by Senebier between 1782–88 to be confined to the green parts of plants which, under the influence of sunlight, convert fixed air (carbon dioxide) into dephlogisticated air (oxygen). His "Mémoires physico-chimiques sur l'influence de la lumière solaire pour modifier les êtres des trois règnes de la nature" in three volumes were published in 1782. The first to formulate a theory, in strictly chemical terms, of vegetable nutrition in his 'tediously prolix' (Sachs) five-volume "Physiologie végétale" (1800), he stimulated his fellow Genevan, Nicholas Théodore de Saussure, to write his "Recherches chimiques sur la végétation" (1804), which was to eclipse his own work. He was a coresponding member of the Institut de France and of the Royal Academy of Turin.

International Commission on Higher Education in Nigeria

Sir Eric Ashby (vice-chancellor of the Queen's University of Belfast and master-elect of Clare College, Cambridge) returned from Lagos on May 7, after attending the inaugural meeting of the International Commission on Higher Education in Nigeria. The Commission (*Nature*, 183, 1231; 1959), with Sir Eric Ashby as chairman, consists of two other United Kingdom members, Dr. J. Lockwood (master of Birkbeck College) and Dr. G. E. Watts (principal of Brighton Technical College); and three American members, Dr. Frank Keppel (dean of the Graduate School at Harvard University), Dr. Eric Walker (president of Pennsylvania State University) and Prof. H. W. Hannah (associate dean of agriculture, University of Illinois). The Nigerian members are Shettima Kashim (formerly Federal Minister of Social Services, chairman of Nigerian College of Technology), Prof. K. O. Dike (vice-principal and professor of history, University College, Ibadan) and Dr. S. D. Onabamiro (senior research fellow in parasitology, University College, Ibadan).

Sir Eric Ashby, speaking at the inauguration meeting in Lagos on May 4, described the decision to set up a Joint Nigerian–United States–United Kingdom Commission as a "Landmark in educational history" as this was the first time that such an international group had been appointed to study higher education in Nigeria. He assured the meeting that the Commission would be able to recommend some of the educational needs of the first twenty years of Nigerian independence could be met, and that it would do its best to prepare for Nigeria something which could be turned into action.

'Procinyl' Dyes

Imperial Chemical Industries, Ltd., has introduced 'Procinyl' dyes, a new class of disperse dyes. It is claimed that the initial four 'Procinyl' dyes display

on nylon and other polyamide fibres the desirable attributes of the established disperse dyes—good levelling, good coverage of irregular-dyeing yarns, good compatibility in admixture, good temperature-range properties and good penetration. They are applied in a similar manner. The essential difference is that the 'Procinyl' dyes are applied initially under slightly acid instead of neutral conditions, and that dyeing is completed by an alkaline fixation stage during which certain reactive groups in the 'Procinyl' dye molecules react chemically and irreversibly with the amine or amide groups in the polyamide fibre and so produce dyeings of high wet-fastness. All forms of nylon and other polyamide fibres, of both the staple fibre and continuous-filament types and including woven piece goods, knitted piece goods and hosiery, can be dyed satisfactorily with the new dyes, which may be applied, as necessary, on the jig (covered jigs for preference), on winches, in paddle dyeing machines and in circulating-liquor machines. The initial four 'Procinyl' dyes—a yellow, an orange, a scarlet and a blue—permit an extensive range of shades to be produced because of the wide inter-compatibility of the new dyes.

Only slight or negligible reaction takes place between 'Procinyl' dyes and acetate and triacetate rayons, for which the new dyes are not expected to be of much immediate interest, although the wet-fastness achieved is generally better than with normal disperse dyes. With the exception of 'Procinyl Yellow G', the dyes are of minor importance on 'Terylene' and other polyester fibres. On 'Acrilan' polyacrylonitrile fibre, although 'Procinyl' dyes build up well to give heavy shades of very high wet-fastness, which results from the reaction between the dye and the basic groups in the fibre, only the yellow is of particular interest, the remaining dyes giving shades of low light fastness. On acrylic fibres not modified by the incorporation of basic substances they display only limited build-up.

British Ceramic Research Association : Mellor Library

THE new library of the British Ceramic Research Association—the Mellor Library—was opened at Stoke-on-Trent on June 16 by Mr. Frank West, vice-president of the Association and a lifelong friend of the late Dr. J. W. Mellor, in whose honour the library has been named. Dr. Mellor, the well-known physical chemist, turned his mind to problems of the ceramic industry ; Wedgwood, a century and a half previously, had transformed a craft into an industry ; Mellor, during the first three decades of the present century, did outstanding service to that industry by giving it the basis of science that had hitherto been largely wanting. As head of the Pottery Department of the North Staffordshire Technical College, Mellor taught a generation of pottery managers ; as first director of research of the British Refractories Research Association (the forerunner of the British Ceramic Research Association) Mellor initiated research at a time when industrial research was a novelty. But perhaps he is best known as the author of the "Comprehensive Treatise on Inorganic and Theoretical Chemistry".

Educational Research

THE third issue of *Educational Research*, the journal of the National Foundation for Educational Research in England and Wales, contains articles on the teaching of mathematics, the ability to teach, the effect of environment on intelligence, school guidance services and a comparison of attainments in different types of primary school. There is also a selected and annotated bibliography of works on the curriculum of the secondary school (Newnes Educational Publishing Co., Tower House, Southampton St., Strand, London, W.C.2. 5*s*. 6*d*.). In the article on the teaching of mathematics, Mr. J. B. Biggs discusses the distaste for school mathematics so commonly reported. His conclusions evaluate the relative effect of basic personality and specific likes and dislikes, particularly in the case of the maladjusted child. Many so-called lazy children are seen to have found an initial block to their number learning because of their temperament. This is heightened by accusations of laziness and consequent unimaginative driving by some teachers. The implications of this and the other stimulating conclusions are important to the teacher who might well ask himself why there is no similar anxiety concerning English.

A New Geological Documentation Service

THE wealth of information available constitutes a serious problem for the future of the research in the Earth sciences. Before 1939, published work could be covered by giving about one thousand references a month. At present, the Service d'Information Géologique of the Bureau de Recherches Géologiques, Géophysiques et Minières indexes monthly more than 3,000 references, and it is estimated that 5,000 references should be given to ensure complete coverage of the field. The situation is complicated by the number of works now appearing in little-known languages, and by the launching of new periodicals and special publications. Faced with this problem, the Service d'Information Géologique of the Bureau de Recherches Géologiques, Géophysiques et Minières, which has taken over and expanded the work of the Centre d'Études et de Documentation Paléontologiques, has set itself the task of providing an extended and rapid service of basic geological information. The Service d'Information Géologique scans every week about 3,500 periodicals, more than 200 of which are published in Russian. The references are typed in the original language or, if they are not in Latin characters, are translated, usually into French ; they are then classified in 1,200 sections under twelve main headings (mineralogy, petrography, stratigraphy, tectonics, geophysics, geological activities, geological phenomena, applied geology, general palæontology, biology, botany and zoology). The work is, of course, carried out under the supervision of scientists. Each reference is indexed by title and by content. The average number of indexes to each abstract card is five.

Central Advisory Water Committee

ON the expiry of the first period of appointment, the Minister of Housing and Local Government, Mr. Henry Brooke, has reviewed the composition of the Central Advisory Water Committee and made various re-appointments and new appointments. The membership of the Committee is drawn from the major interests concerned with water, for example, water supply, industry, scientists, agriculture, river boards. The Minister is chairman of the Committee, and the vice-chairman is the Parliamentary Secretary, Mr. J. R. Bevins. Since its reconstitution in 1955 the Committee has published reports on the demand for water in England and Wales, on information on water resources and on the law dealing with the disposal of trade effluents.

Seismological Association Meeting in Toronto

The report of the meetings of the Section for Seismology and the Physics of the Earth's Interior, prepared by the associate secretary, Dr. Markus Båth, of Sweden, has recently been published (pp. 448. Strasbourg: Bureau Central International de Séismologie, 1958). Most of the subdivisions into which this subject may be divided were discussed in the twenty-two sessions. Detailed reports of these meetings, the presidential address by Prof. K. E. Bullen, of the University of Sydney, the report of the meeting of the European Seismological Commission, the Committee of the International Seismological Summary and the Committee for the International Geophysical Year are included. In addition, there are seismological reports from thirty-four countries, and the resolutions adopted at the assembly. The whole covers some 455 quarto pages. At the conference, ten sessions were devoted to seismology alone, six to joint meetings with the Association of Volcanology and two to joint meetings with the Association of Geodesy. It was at an extra session at Toronto that Prof. K. E. Bullen announced that the U.S. Atomic Energy Commission had released information concerning the time and place of a future underground nuclear detonation in Nevada, so that seismologists could prepare to participate in the recording. The International Geophysical Year Committee discussed particularly the recording of earthquakes with epicentres in the arctic and antarctic regions; and it is noteworthy that M. E. Guyot is proceeding with the preparation of a seismological dictionary which it is hoped will be published without delay.

Soil Survey of Great Britain

The soil survey of Great Britain, with headquarters at Rothamsted, will occupy many years, and reports are to be published as each county is completed. The magnitude of the task can be realized from the memoir on Anglesey (Agricultural Research Council. Memoirs of the Soil Survey of Great Britain—England and Wales. The County of Anglesey: Soils and Agriculture. By E. Roberts. Pp. viii + 116 + 11 plates. London: H.M. Stationery Office, 1958, 10*s*. net), which includes also a small proportion of Caernarvonshire; nearly fifty soil series, which are the mapping units, are identified and described. Anglesey is relatively flat, but there are considerable variations in the land surface due to the rugged outcrops of the Mona complex, the sharp escarpment of the Carboniferous limestones, the igneous rocks, wind-blown sands and glacial features. The varying thickness of the boulder clay has contributed to the irregular undulations of most of the fields.

Classification and mapping of the soils are based on the soil profile, since it reflects the action and balance of the many processes that have led to its formation; drainage has a profound effect, and is taken into account in the classification. Although familiar to soil scientists and to many advisory officers, the subject is new to workers in related subjects, and to farmers. The Soil Survey of Great Britain will be the foundation for a planned approach to fertilizer and cropping problems for many years, and such reports will have to be studied, and the maps referred to frequently. The one inch to the mile soil map that is provided may prove too small for reference to some individual farms on or near the margins of the soil areas, but a 6-in. map is available for reference at Rothamsted.

Grassland Productivity

"The Measurement of Grassland Productivity" was the subject of the sixth Easter School in Agricultural Science which was held at the University of Nottingham School of Agriculture, Sutton Bonington, during April 13–16, and was organized by Prof. J. D. Ivins. Twenty papers were read, primarily concerned with techniques of grassland evaluation. Assessment of productivity from the botanical point of view, in terms of animal production, the consumption of herbage by grazing livestock and grassland productivity on a farm scale were considered. New varieties of herbage plants have been produced and their requirements have been explored to a great extent. New techniques have been developed which have resulted in vast increases in the production from grassland, but a constant problem and hindrance to development has been—and still is—the lack of methods which may be used with validity to measure and compare grassland productivity. Some 140 members from Britain and overseas exchanged experiences and ideas and discussed the limitations and applications of techniques of measuring the productivity of grassland. The proceedings will be published.

Safety in Mines Research

The thirty-sixth annual report on Safety in Mines Research (pp. 81 + 4 plates. London: H.M. Stationery Office, 1958. 5*s*. net) is a general review of progress in the year 1957 of the Safety in Mines Research Establishment of the Ministry of Power. The report describes research undertaken in the general fields of explosives and blasting devices, explosion hazards, breathing apparatus, fire hazards, engineering and metallurgy, dust control and pneumoconiosis hazards, and in certain other fields, together with a record of testing services carried out by the Establishment. A significant feature of some aspects of the work is the active co-operation and interchange of results with kindred establishments in France, Germany and Poland. More than ninety topics are discussed; it is difficult to select individual topics for special mention, but perhaps attention may be directed to the work reported on the fluid mechanics of coal dust explosions, a subject of interest to all concerned with fires and explosions due to organic dusts. There are, in fact, many topics reported which are of interest and importance to several industries in addition to the mining industry, including breathing apparatus, engineering and metallurgical problems of importance in conveying, winding and supports, and the study of dusts and of pneumoconiosis.

Morbidity Statistics from General Practitioners

In the series of Studies on Medical and Population Subjects, the first volume of morbidity statistics collected from general practitioners has recently appeared (General Register Office. Studies on Medical and Population Subjects No. 14: Morbidity Statistics from General Practice, Vol. 1 (General). By Dr. W. P. D. Logan and A. A. Cushion. Pp. iv + 174. London: H.M. Stationery Office, 1958. 15*s*. 6*d*. net). A number of practitioners agreed to keep records of all consultations with patients on their list, and the General Register Office went to considerable trouble to obtain the correct population at risk to which these consultations could be related. While the practices were not chosen as a representative sample of the total population, this is the

first time that a survey has been taken, and that data showing the load on general practitioners have become available on this scale. The present publication shows consultation rates, and rates of patients consulting for different age and sex groups and different diseases. It is expected that a further volume which will contain figures on occupational morbidity will be issued in the future.

Mammals of the Belgian Congo

A PAPER by J. Verschuren on the ecology and biology of the larger mammals of the Garamba National Park in the north-east of the Belgian Congo forms the ninth fascicle of the results of H. de Saeger's expedition for the exploration of the park (Exploration du Parc National de la Garamba : Mission H. de Saeger. Fascicule 9 : Écologie et Biologie des Grands Mammifères (Primates, Carnivores, Ongulés). Par Jacques Verschuren. Pp. 225 + 2 planches. Bruxelles : Institut des Parcs Nationaux do Congo Belge, 1958). In the region studied the larger mammals are much more difficult to observe than in East Africa owing to the much denser vegetation in which they seek refuge, but the author has made good use of the two years that he was in the field and has collected much valuable information about their biology. After a short introduction describing the country and the methods employed the work is arranged systematically, and each species is dealt with under the headings : particulars of specimens examined, local names, geographical distribution, systematics and morphology, and ecology and biology. For most species the last section is by far the largest and is full of carefully recorded observations of the greatest interest. Fifty-one species are dealt with, distributed among the Primates, Pholidota, Carnivora, Tubulidentata, Proboscidea, Hyracoidea, Perissodactyla and Artiodactyla. The author adds that his lengthy experience of mammals in the wild has convinced him of the invalidity of many of the innumerable forms, subspecies, and races that have been so profusely described by some writers—a remark that will be heartily endorsed by other field zoologists. The value of the paper is enhanced by a large number of photographic illustrations, including two plates in colour.

Collision Broadening of Spectral Lines

COLLISION broadening is an important process in the formation of stellar absorption lines, and collision shifts have been discussed as a possible explanation of that part of the red shift of solar lines which is unaccounted for by the Einstein gravitational shift. W. R. Hindmarsh (*Mon. Not. Roy. Astron. Soc.*, **119**, 11 ; 1959) has recently reported the results of the first of a series of measures of collision effects in atomic spectra. The collision shift and broadening of the neutral calcium line λ 4227 A. due to an external pressure of helium have been measured. The line was formed in absorption by passing white light through calcium vapour in the presence of helium at various pressures less than one atmosphere. The half-intensity damping width of the line was found to be $1{\cdot}72 \times 10^{-20}$ cm.$^{-1}$ per atom per cm.^{3} of helium, and the shift $0{\cdot}05 \times 10^{-20}$ cm.$^{-1}$ per atom per cm.^{3} towards the violet. The ratio of broadening to shift on the Lindholm theory is 2·76, and the shift is predicted to be towards the red. The observed ratio is much larger and the observed shift is in the opposite direction. This discrepancy must be due to the involvement of the short-range repulsive forces between calcium and helium atoms as well as the long-range van der Waals forces. Hindmarsh also shows that the collision shift of the calcium line is a negligible component of the solar red shift and cannot account for the difference between observed and predicted solar red shifts. In the second paper following the above, W. R. Hindmarsh and K. A. Thomas show that for two argon lines the collision shifts are in reasonable agreement with the Lindholm theory.

Hot Laboratory Equipment

"HOT Laboratory Equipment" is a revised and enlarged second edition of the "Hot Laboratory Catalogue", which constituted the major portion of "Chemical Processing and Equipment" (*TID*-5276), published by the U.S. Atomic Energy Commission as one of the several volumes for the 1955 International Conference on the Peaceful Uses of Atomic Energy. The new edition (pp. viii + 429. Washington, D.C. : Government Printing Office, 1958. 2.50 dollars), which is fully illustrated, contains descriptions of facilities, equipment and accessories for handling moderate to large amounts of radioactive materials. It lists 229 items compared with 126 in the first edition, and includes newly developed items as well as items omitted for various reasons from the first edition. Acknowledgment is made wherever possible to the organization responsible for the development of the particular equipment described. Most of the equipment listed was developed by national laboratories or contractors to the Commission, but some were developed by private firms. The contents is confined to hot laboratory equipment produced in the United States, but the reader is referred in the preface to two British publications ("Remote Handling Equipment", by A. Apperly, Atomic Energy Research Establishment, *E/R* 1291 ; and "Radioisotope Instrumentation and Accessories", by D. Taylor and A. G. Peacock, Scientific Instrument Manufacturers' Association, 1955) for information on similar equipment available in Great Britain.

Textiles and Dyes at the University of Leeds

THE eighty-fourth report of the Textile Industries and Dyeing Advisory Committee on the work of the Departments of Textile Industries and Colour Chemistry and Dyeing in the University of Leeds (pp. 47. Leeds : The University, 1959) covers the session 1957–58, in which applications for admission greatly exceeded places and very full programmes of teaching and research were maintained. In the Textile Industries Department, full-time students numbered 351 and in that of Colour Chemistry and Dyeing 50. Lists of publications are included. In textile physics work continued in X-ray diffraction, electron microscopy, infra-red absorption, and sedimentation in the ultracentrifuge. A second electron microscope was installed. In textile chemistry a method of producing a permanent lustre on all-wool fabrics has been developed and the chemical mechanism of permanent set, especially that obtained with sulphite–bisulphite solutions, was re-examined. Work on the effect of variations in the nature of the keratin in the assessment of wool quality continued. The constitution of some suint pigments which may be involved in the staining of wool, the surface activity of steroids and pyrolytic degradation of cholesterol are being studied, and a brief examination of the dielectric properties of lanosterol indicated its suitability for use in impregnated paper capacitors.

In textile engineering good progress is reported in the analytical study of loom noise and in a study of the drying of textiles. In textile technology, work on the chemistry and practice of finishing fabrics made from both wool and man-made fibres continued and on the measurement of yarn irregularity. The chemical properties of pigmented wool, the action of concentrated sulphuric acid on wool, the removal of compounds of high molecular weight from textile materials and the degradation and yellowing of nylon were also studied.

In the Department of Colour Chemistry and Dyeing the course of the changes which occur in the reaction of aromatic carbonyl compounds with basic substances was examined, a study of stilbenequinone and its derivatives was completed, and work on elimination of groups from vat dyes on reduction and on the reactions of sulphinic acids with azo compounds and azines continued. A group of diazonium salts soluble in benzene was prepared, and a study of the interaction of aminoanthraquinones and aminofluorenanes with nitrobenzene and α-nitronaphthalene was completed, as well as work on the vapour pressure and absorption energies of some anthraquinone and azo dyes. The influence of the acetyl value of acetate rayon on the rate of dyeing and affinity for disperse dyes is being studied.

Journal of Nutrition

Dr. Richard H. Barnes, dean of the Cornell University Graduate School of Nutrition, Ithaca, New York, has been appointed editor of the *Journal of Nutrition*. He succeeds Dr. George R. Cowgill of the Yale Nutrition Laboratory, who has served as editor for twenty years. Dr. Cyril L. Comar, director of the Laboratory of Radiation Biology, New York State Veterinary College, has been appointed associate editor. The appointments became effective July 1, 1959. The editorial offices of the *Journal of Nutrition* are being moved from Yale University to the Cornell University campus. Manuscripts should be sent to Dr. Barnes at the Graduate School of Nutrition, Savage Hall, Cornell University, Ithaca, New York.

Nature Conservancy Awards for 1959

The Nature Conservancy announces the following awards of research studentships for postgraduate training in ecology, tenable for periods up to three years at the universities shown: *Botany:* J. K. Marshall (Cambridge), D. P. Nicholas (Liverpool), W. J. Roff (Cambridge), J. T. R. Sharrock (Southampton), D. T. Streeter (London); *Zoology:* M. L. Clark (Leeds), E. R. Creed (Oxford), J. M. Edington (Durham), C. J. Henty (Oxford), J. B. Nelson (Oxford), G. C. Phillips (Oxford); *Geography:* I. G. Simmons (London).

University News: Edinburgh

Prof. A. D. Ritchie, professor of logic and metaphysics in the University of Edinburgh, retires on September 30; his long and distinguished career was mentioned in reviewing his recent book, "Studies in the History and Methods of the Sciences" (*Nature*, July 4, p. 4). Prof. E. E. Harris, formerly professor of philosophy in the University of the Witwatersrand, has been appointed acting head of Prof. Ritchie's Department for one year.

Swansea

The following appointments have been made in the University College of Swansea for the session 1959–60; Dr. J. R. Cross, superintendent of the Chemistry Laboratories; Miss Glenys Thomas, map curator and cartographer in the Department of Geography; Mr. P. W. Davies, assistant lecturer in metallurgy; Dr. H. E. Evans, lecturer in engineering; Mr. B. W. Preece, assistant lecturer in engineering.

Announcements

Mr. Walter Garner, formerly chairman of the Yorkshire Section and at present chairman of the London and District Section of the Textile Institute, and Dr. A. R. Urquhart, honorary secretary of the Institute and an assistant director of the British Cotton Industry Research Association, have been awarded the Service Medal of the Textile Institute.

Prof. H. Mark, director of the Polymer Research Institute of the Polytechnic Institute of Brooklyn, New York, will deliver the Fourth Baekeland Memorial Lecture under the title "Recent Progress in Polymer Chemistry". The Lecture will be delivered on October 22 at the Royal Institution, Albemarle Street, London, W.1.

The International Commission on Zoological Nomenclature has been given accommodation in the British Museum (Natural History). This will greatly facilitate the work of the Commission by reason of the unique library facilities and wide range of specialist advice available. Correspondence should in future be addressed to Mr. N. D. Riley (Honorary Secretary), International Commission on Zoological Nomenclature, c/o British Museum (Natural History), London, S.W.7.

The second session (1959–60) of the Welsh Soils Discussion Group will open with a meeting in the Department of Agricultural Chemistry, University College, Bangor, on October 28. The subject for discussion will be "Mineralogical Aspects of Soil Science"; the introductory speakers will be Dr. F. Smithson and Mr. R. I. Davies (Bangor) and Mr. D. F. Ball (Nature Conservancy, Bangor). Further information can be obtained from Mr. J. A. Taylor, Geography Department, University College, Aberystwyth.

The Scottish Conference on "Relationships in Industry: Some Changing Concepts of Management", which is being organized jointly by the British Institute of Management and the Ministry of Labour, will be held at Gleneagles Hotel during October 23–24. It will be opened by Sir Alexander Fleck, chairman of Imperial Chemical Industries, Ltd. Further information can be obtained from the British Institute of Management, Management House, 80 Fetter Lane, London, E.C.4.

In November 1859 Charles Darwin published "The Origin of Species" and Queen Victoria granted the Royal Title to the Royal Society of Victoria. To mark these two centenaries, the Society is organizing a symposium on the Evolution of Living Species, to be held in Melbourne during December 7–11. Dr. Ernest Mayr of the United States will be the guest speaker. Further information can be obtained from the Honorary Secretary, Royal Society of Victoria, 9 Victoria Street, Melbourne, C.1, Victoria.

Referring to the review in *Nature* of June 27, p. 1766, Messrs. Chapman and Hall state that the present American price of Cox's "Planning of Experiments" is 7.50 dollars.

MOLECULAR AND ATOMIC MOTIONS BY RADIO-FREQUENCY METHODS

MAXWELL-A.M.P.E.R.E. CONFERENCE

A JOINT meeting of the Colloque A.M.P.E.R.E. (Atoms et Molecules par Etudes Radio-Electriques) and the British Radio Frequency Spectroscopy Group was held during April 1–3 at Queen Mary College, University of London. The meeting was attended by more than two hundred scientists, mostly from the British Isles but with strong representation from France, Holland, Switzerland and the Eastern European countries in particular. The subject for discussion at the Conference was, "Molecular and atomic motions in liquids and solids by radio frequency methods". In the tradition of the A.M.P.E.R.E. meetings the subjects covered were, dielectrics, nuclear magnetic resonance, quadrupole magnetic resonance and electron spin resonance. However, the range of the papers was constrained somewhat more than has been usual at the A.M.P.E.R.E. conferences by the specification of a subject for discussion, albeit rather widely interpreted.

The forty-four papers presented showed the power and range of the radio-frequency methods in studying molecular and atomic motion and there was an impressive consistency and similarity in the information produced by the very different experimental methods. It was regrettable that time did not allow the inclusion of mechanical and ultrasonic absorption measurements although these received mention in several of the papers.

Since many people versed in one discipline attended lectures in another, the occasion was a suitable one for having a general introductory lecture in each subject, and these were given by Prof. H. Fröhlich (Liverpool) on "Dielectric Theory", Dr. J. G. Powles (London) on "Motional Effects in Nuclear Magnetic Resonance" and by Dr. M. Buyle-Bodin (Grenoble) on "Motional Effects in Pure Quadrupole Resonance". Even so, many of the discussions became extremely technical and specialized and the difficulty in having a meeting on a subject which cuts across the traditional interests and compartments of science was apparent. This difficulty is a common one in conferences these days although highly specialized discussion is said to be evidence of 'maturity' of a subject. It is regrettable that the cross-fertilization which should be brought about by conferences such as this one is so difficult to achieve. It is therefore very valuable to have organizations 'd'informations mutuelles' such as the Colloque A.M.P.E.R.E. and the British Radio Frequency Spectroscopy Group, the membership of which cuts across the traditional disciplines and contrasts with the extreme specialization of many organizations.

It was a source of great sorrow to all present, and particularly to the writer, that Prof. Freymann (Paris), the inspiration of the Groupement A.M.P.E.R.E., was unable to be present owing to illness, and that this should be the first A.M.P.E.R.E. Conference he has missed.

The conference overcame in large measure the difficulties occasioned by the fact that it was held outside France for the first time (apart from a foray to Geneva in 1957) and was well attended by French scientists. Although some 50 per cent of the papers were presented in French, the British members appeared to survive the ordeal without severe discomfort, and it may be that the teaching of French in our grammar schools is not as ineffective as is commonly supposed. The language difficulty was lessened by the provision of pre-prints of most of the papers.

It would obviously be impracticable to mention all of forty-four papers and a brief summary only will be presented in an attempt to give some idea of the scope of the conference.

The conference was opened by Prof. H. Fröhlich, who gave a masterly summary of the present situation in the theory of dielectrics, the main point of which was that the whole of the general theory has been worked out. The continuing appearance of papers on 'general theory' are no more than mathematical exercises, and whether these results are correct or not they are irrelevant. This point of view was undoubtedly novel to many present. He elaborated his position by discussing the whole field of dielectric loss in which he distinguished four types all but one of which are well understood. He was particularly concerned with the extent to which the theory can be dealt with macroscopically, which is of first importance because of the long-range nature of dipolar forces, and with the number of independent parameters required for an *understanding* of the phenomena involved. He did point out nevertheless that a great deal of work remains to be done in the theory of dielectrics but that this should be concerned with the detailed interpretation, using models and so forth, and in the search for information about materials and processes.

This lecture led on naturally to the more detailed discussion of a number of papers on dielectric loss in liquids and solutions, which depends in large measure on molecular properties and in which the 'model' aspect was very evident.

J. D. Hoffman (National Bureau of Standards, Washington) introduced a session on solids with an account of his work on systems having multiple relaxation times leading to bimodal, or even multimodal, loss curves which he explains in terms of multiple minima in the energy as a function of the orientation of a dipole. A paper by H. Gränicher and C. Jaccard (Zurich) summarized the present position in the interpretation of the dielectric properties of ice. B. Szigeti (Liverpool) described his recent work on a so far unobserved librational absorption process which should be found in crystalline long-chain substances.

There were a number of papers on the dielectric properties of systems in which water or a gas was adsorbed on materials such as silica gel.

The session on nuclear magnetic resonance was opened by J. G. Powles (London), who gave a summary of motional effects which can be studied by nuclear magnetic resonance, including numerous examples of the various types of effect which may occur. He pointed out that examples of many of these would be found in the following papers but gave a number of extra ones in order to provide a balanced picture of the potentialities of the method.

There were several papers on motional effects in hydrocarbons which were concerned with the elucidation of the molecular motions occurring in these molecular crystals. E. R. Andrew (Bangor) summarized his recent work on macroscopic motional effects, extending his considerations to quadrupolar effects and showing in particular how macroscopic motional experiments may help in deciding the nature of a magnetic interaction. A paper by K. Luszczynski (London) discussed the rather complex motional effects in the polymer poly*iso*butylene. J. A. E. Kail and J. G. Powles (London) had studied the molecular motion in *iso*butyl bromide, which is of interest since it is readily obtained either as a crystal or as a supercooled liquid over a wide temperature-range. The value of nuclear magnetic resonance measurements made at kilocycle frequencies was pointed out by G. Hochstrasser (Geneva). The interest in comparing nuclear resonance and self-diffusion parameters in mobile liquids of long-chain compounds was discussed by D. Cutler and J. G. Powles (London). M. P. McDonald (Heston) presented high-resolution results on amphiphilic solutions which have liquid crystal phases. D. J. Kroon and C. v. d. Stolpe (Eindhoven) reported nuclear resonance measurements which throw light on the movement of hydrogen in the alloy Th_2Al, which is used as a getter. H. Winkler (Leipzig) discussed the nuclear resonance of water sorbed on alumina, which links up nicely with the corresponding measurements reported in the Dielectrics Session by G. Ebert (Leipzig). I. Solomon (Saclay) reported a new method of measuring long nuclear resonance relaxation times.

The session on pure quadrupole resonance was opened by M. Buyle-Bodin (Grenoble), who gave an excellent summary of the motional effects which are to be found and included an appreciation of his own valuable contributions in this field. J. L. Ragle (Amherst, Mass.) reported work which indicated the motional effects in 1,2-dichloroethane. It was reported by F. Herlach, H. Gränicher and D. Itschner (Zurich) that a new phase transition had been found in potassium iodate by nuclear quadrupole resonance, and the value of this method in detecting such 'weak' transitions was pointed out.

Time was then given to an informal discussion on commercial instrumentation in magnetic resonance. A number of firms briefly described their products and this was followed by a general discussion. The time and occasion were appropriate since the amount of commercial instrumentation available is at present rapidly increasing. It was of interest to note the great difference in tone and objectivity between a commercial and a scientific discussion.

In the session on electron spin resonance it was evident that motional effects are less important and appear very much as a by-product. D. J. E. Ingram, M. Fujimoto and M. C. Saxena (Southampton) reported experiments indicating two types of motion: one in which rate of radical diffusion in an organic glass could be measured, and another in which the spectrum differed with temperature, which was taken to indicate an effect due to reorientation of methyl groups within the radical. It was unfortunate that no paper was offered in which the motional averaging of the anisotropic hyperfine splitting was discussed. In a striking paper, K. H. Hausser (Heidelberg) showed how the resolution of hyperfine spectra in free-radical solutions depends on the optimum condition for observation of detail in the spectrum, which is essentially a motional effect and which must be arranged to give optimum relaxation parameters. Presumably motional effects can be studied in this way although this was not emphasized in the paper. A. Landesman (Saclay) reported a study of the $(SO_3)_2NO^{2-}$ ion in solution by measurement of the solvent protons.

During a session on motional effects in irradiated materials, J. S. van Wieringen and A. Kats (Eindhoven) reported paramagnetic resonance spectra of irradiated fused silica at liquid-nitrogen temperature which were due to hydrogen atoms formed from water impurities. The variation of these signals with temperature and time was used to study the motion of the hydrogen atoms. A. Lösche (Leipzig) reported proton magnetic resonance measurements on nylon-6 which had been subjected to doses of comparatively weak γ-radiation over periods of several months. The radiation causes chemical changes which affect the molecular mobility of the polymer and hence the nuclear signals. It was suggested that this might be a suitable method of measuring integrated radiation doses when the intensity is rather low.

The papers presented at the conference, but not the discussions, are being published in a special issue of *Archives des Sciences* (price 25 Swiss francs). Copies may be obtained by writing to the Secretariat A.M.P.E.R.E., Institut de Physique, Bd. d'Yvoy, Geneva, Switzerland.

The next Colloque A.M.P.E.R.E. will be held in Pisa, Italy, in September 1960. J. G. Powles

SEMICONDUCTING SILICON CARBIDE

One of the most important aspects of semiconductor physics in recent years has been the search for materials which yield devices capable of operating at higher temperatures than germanium and silicon. In this search, silicon carbide has been regarded as an important candidate, although, indeed, there are others. For silicon carbide, the high temperature of formation implies a high degree of stability at all temperatures likely to be encountered by devices. Moreover, the material can be regarded simply as silicon in which half the atoms have been replaced by the chemically similar carbon. In this way, much of the available information concerning, for example, the effect of impurities in germanium and silicon should be applicable to silicon carbide also, considering that the bonds are almost wholly covalent. Again, the relatively wide band gap would promise a large measure of electrical stability over a wide range of temperature. These advantageous features tend, unfortunately, to be balanced by a major practical difficulty, namely, that of growing single crystals with a controlled content of additives and crystal defects.

In order to explore these problems and to make a general assessment of our present knowledge, a major conference was recently held at Boston during

April 2–3, sponsored by the U.S. Air Force Cambridge Research Center and under the chairmanship of Dr. J. R. O'Connor. The U.S. Air Force Cambridge Research Center has for some time been the principal agency engaged on the task of initiating, supporting and co-ordinating a comprehensive research programme on silicon carbide, covering fundamentals and devices on a long-term basis. Forty-six papers were presented, dealing with such matters as the phase relations of the silicon – carbon system, methods of crystal preparation (by sublimation, gaseous cracking, epitaxial growth and from solution), silicon carbide as a solid (crystal structure, surface morphology, oxidation), silicon carbide as a semiconductor (band structure, electrical and optical properties) and silicon carbide devices.

Recent phase studies show that silicon carbide does not decompose thermally below 2,830° C., contrary to earlier reports. Large single crystals of the material have, of course, been available for a long time; but, as a rule, these appear only accidentally in the course of manufacture of silicon carbide in large furnaces which do not permit accurate control. In comparison, the laboratory methods listed above lead to crystals of much higher purity (for example, as assessed by neutron activation and spectrographic methods) but of very much smaller size. It has been widely suggested that the scale of the operation may have an important influence on the outcome and that, in any event, the temperature gradient in the direction of growth should be brought under control. Crystal growth from solutions of silicon or iron – silicon alloys supersaturated with carbon has yielded plates up to 8 mm. across and 0·5 mm. thick. The optimum growth conditions have not yet been determined. The structural studies are, of course, devoted to the well-known property of silicon carbide of forming a great variety of polytypes which are not yet fully understood. There is as yet no evidence of any definite connexion between polytype formation and impurity content, but interesting relationships are known to exist between the polytypic structure and the geometry of the spiral growth surfaces.

The width of the forbidden energy gap, derived from optical absorption measurements, has been found to be 2·86 eV. at 300° K., with a temperature coefficient of $-3{\cdot}3 \times 10^{-4}$ eV. deg. C. The existence of impurity bands has been inferred from observations of electroluminescent spectra as a function of temperature and current density. The electroluminescence itself is now firmly believed to be due to the injection of minority carriers through p–n junctions and their subsequent recombination in luminescent centres, even though many details still remain to be clarified. An electron mobility of 32 cm.²/volt-sec. has been quoted for material containing 10^{15} to 10^{17} donors/cm.³.

The question of departures from stoichiometry is still highly controversial. It is not yet known whether such departures exist to any significant extent and whether they lead to donor or acceptor formation if they do. The minority carrier lifetime, measured by observing the photoconductive decay following the cessation of an optical stimulus, is very short but can reach a few tenths of a microsecond. This fact, coupled with the relatively small carrier mobility, makes the design of silicon carbide transistors a problematical prospect. It is, however, believed that such transistors, whether unipolar or bipolar, could now be made if the best available crystals were used in conjunction with the most sophisticated micromanipulation techniques. In practice, gallium phosphide, with its lower melting-point ($\sim$ 1,340° C.), wide band gap (2·25 eV.) and higher carrier mobilities may prove to be an important competitor. Apart from this, there are fair prospects for device applications in the field of high-temperature rectification. p–n junctions can be prepared by the usual doping techniques and a finished encapsulated rectifier capable of operation at 500° C. was described. The more familiar application of silicon carbide for the manufacture of non-linear current devices ('varistors') is still of great interest. The behaviour of these devices is now reasonably well understood, even though the detailed circumstances may be complicated by thermal effects, impact ionization and the current-dependent charges in intergranular surface states.

The proceedings of the conference were summarized by a review panel under the chairmanship of Dr. W. Shockley. They will be published in book form by Pergamon Press.

H. K. Henisch

AVAILABILITY OF PLANT NUTRIENTS

A MEETING of the British Society of Soil Science held, by kind permission, at the London School of Economics on April 9, was devoted to consideration of the factors which determine the availability of nutrients in the soil. Five papers were presented and discussed.

Dr. R. K. Schofield (University of Oxford) referred to the successive stages in transfer of nutrients from the soil surfaces, through solution to the roots where metabolic assimilation takes over; any one stage may provide a limiting factor in the supply to the plant and the problem is to unravel their relative importance. Extraction with a weak electrolyte such as calcium chloride goes some way towards characterizing the intensity factor of phosphorus in the soil, but use of phosphorus-32 and calcium-45 has given a better understanding of the labile pool of these nutrients and a measure of the capacity factor. The low concentration of phosphorus extracted by calcium chloride compared with the amount isotopically exchangeable suggests that the time of transit between absorption sites is small. Uptake by roots introduces another factor, but pot experiments with cabbages, barley and lupins using phosphorus-32 showed no differences in the supplies accessible to these plants. Judged by the specific activity of the phosphorus in the plants and in various soil extracts, calcium chloride solution or water gave a better assessment of availability than did many of the solutions often used in soil analysis; these liberated phosphorus which was not available to plants.

Dr. P. Newbould (University of Oxford) described experiments with calcium-45 uniformly mixed with

two soils in pots. The specific activity of calcium absorbed by barley and ryegrass fell steadily during growth owing to a slow equilibration with forms of calcium other than exchangeable calcium. As roots locally depleted supplies of labile calcium, more calcium came into circulation. Exchangeable and available calcium can no longer be regarded as synonymous, and the latter is affected by the activities of plant roots.

Dr. R. Scott Russell (Agricultural Research Council Radiobiological Laboratory) directed attention to different steps in nutrient absorption by roots and stressed that the effective area of absorption was restricted to a region near the apices. The availability of a nutrient to a plant may be influenced by interactions with other ions either by competition or by physiological changes. Dr. Scott Russell referred to work which suggested that the individual root-absorption characteristics of different crops influenced the apparent availability of a nutrient such as phosphorus in a soil.

The probable parts played by micro-organisms were described by Mr. J. S. Waid (Levington Research Station, Ipswich), who stressed that much of the evidence was circumstantial and required further substantiation. Organisms are known to be able to increase the water solubility of nutrients by oxidation or reduction, and by the decomposition of organic materials; the availability of nitrogen is intimately bound up with biological processes. Soil organisms may compete with roots for soluble nutrients especially when stimulated by supplies of organic materials, some of which may be provided by the roots themselves; production of carbon dioxide or toxins may affect the physiological activity of plant roots.

Dr. G. W. Cooke's paper (Rothamsted Experimental Station) described the problems of assessing the nutrient status of a soil for advisory purposes: here the criterion is the probable economic response of various crops to fertilizer dressings, and in this field soil analysis has not made much progress. The results generally distinguish between the broad levels of nutrient status for phosphorus and potassium, but in order to avoid crop failure in the exceptional cases the overall application of these fertilizers is about double the amount that is economically justified. The assessment of the nitrogen status of soils is even more uncertain, and there is an acute need for the development of fresh analytical techniques tested against field trials. Dr. Cooke suggested that a more successful approach might lie in the use of soil analysis for 'fertility control' whereby a record was maintained of the fertility status of a soil so that warning was given of abnormalities before they became acute.

In the open discussion which followed these papers the following points were among those made.

Correlation between soil analyses and field responses is poorer in tropical and other under-developed areas than it is in Britain, yet the need for reliable soil tests is even greater. Different speakers stressed the importance of studying the anomalous soils in order to discover which factors affecting the availability of nutrients have been neglected. Analysis should not be divorced from examination of profiles since often these showed some physical property which meant that, while nutrients might be available in the chemical sense, they were inaccessible to plant roots.

The value of plant analysis in relation to fruit crops and forestry was mentioned; by this means it may be easier to recognize an interaction effect which is not revealed by soil analysis. Some progress was also reported on the development of techniques for determining the nitrogen status of soils: this seems to be greatly affected by re-wetting of air-dry samples.

D. V. Crawford

AHMEDABAD MILLOWNERS' TEXTILE INDUSTRY'S RESEARCH ASSOCIATION

A TEXTILE research laboratory, created and sustained by the co-operative effort of the industry and the Government of India, was envisaged by the Ahmedabad Millowners' Association as early as 1944. In 1947, the Ahmedabad Textile Industry's Research Association was registered with a membership of seventy-one mills. Ahmedabad thus became the proud pioneer in establishing a co-operative research centre for the cotton textile industry in India.

The Association started functioning in 1949, and its impact was soon felt by the industry in and around Ahmedabad. It became clear to the original members that the benefits accruing from research could with advantage be placed at the disposal of the industry on a nation-wide basis. With this object in view, the constitution of the Association was suitably amended so that mills outside Ahmedabad could become members and enjoy the same research benefits as the original founders. The present strength of members including all categories stands at eighty-eight mills and allied concerns, comprising thirty lakhs of spindles and sixty-three thousand looms—roughly one-third of the Indian cotton textile industry.

The policies of the Association are decided by an autonomous body known as the Council of Administration. At present, the twenty-member Council is made up of representatives of management, nominees of the Government of India, the director and secretary of the Association as well as directors of other research organizations, and co-opted scientists. The Textile Commissioner is one of the nominees of the Government of India. Shri Kasturbhai Lalbhai has been the chairman of the Council from its inception.

The composition of the Council ensures a balanced and co-ordinated research policy which takes into account similar efforts by other textile research institutions and national laboratories. Further links with Government and with national research in related spheres have been established through the Ministry of Scientific Research and Cultural Affairs.

The Association began modestly in 1949 in three rooms in the Mafatlal Gazalbhai Science Institute. The foundation stone of the present building, which is housed on a 50-acre campus to the west of Gujarat University, was laid by Sardar Vallabhbhai Patel in November 1950. The building was completed towards the end of 1953 and formally declared open by Shri Jawaharlal Nehru in April 1954.

The laboratories of the Association are equipped with instruments for research in textiles and allied fields. Some of these instruments have been designed and fabricated there. The physics laboratory has equipment for studying the structure and physical and mechanical properties of fibres, yarns and fabrics. The chemistry laboratory has, in addition to the usual facilities for analysis of textile materials, a unit processing section equipped for the treatment of samples of yarns and fabrics through processes such as bleaching, dyeing, printing and finishing. The pilot mill is a versatile unit and its machinery offers a wide range of processing sequences in spinning, weaving and chemical processing. The workshops are equipped for the dual purpose of servicing mill machinery and of designing, fabricating and servicing laboratory instruments.

The Association owes its success in large measure to the enthusiasm of its workers. Most of these workers have been recruited from universities and initiated into specialized fields of industrial research. When necessary, training has been supplemented by periods of study in overseas institutions. Technical assistance schemes such as the Point Four Programme, the Colombo Plan and the Imperial Chemical Industries Fellowships have been of great value. From a small group of about twenty-five workers in 1949, the Association has developed into an organization with a total strength of 200, which is made up of 75 scientists and technologists, 25 administrative workers, 40 skilled operatives and 60 service personnel.

The services of a number of foreign specialists have been secured from time to time with the assistance of organizations like Unesco and the International Labour Organization; in 1956 the Association was recognized by Gujarat University as a teaching centre for postgraduate research. At present most of the research students are awarded scholarships or fellowships by the Government of India, the Council of Scientific and Industrial Research, Gujarat University and the Association.

In a technologically under-developed country, it is often the path of least resistance to apply to one's own use the findings of more advanced countries. During the early days, the Association emphasized the application of scientific and technical knowledge already available to the problems of the industry. This practice of helping the industry to implement the findings of research has paid rich dividends and constitutes one of the main activities of the Association at present. In the process, industry has become wide awake to the potentialities of original research and has cordially welcomed the Association's efforts.

While being primarily a research organization the Association tries to help industry in other ways. Training in various skills, such as management and supervision, statistical methodology and testing procedures, is given to the staffs of member mills. Such trained personnel not only become better equipped for their work, but also help in securing more effective implementation of the Association's programmes. Often, they form the nucleus of research and training groups in their own organizations.

GLASSHOUSE CROPS RESEARCH INSTITUTE

THE annual report of the Glasshouse Crops Research Institute for 1957* shows that, although full facilities are not yet available, the physical development of the Institute has made good progress and some of the major problems associated with commercial glasshouse practice have been investigated. Physiological studies of the growth of tomatoes have continued, and practical problems of plant spacing and pruning have received attention. Previous studies at Cheshunt and the Institute havn shown that retention of lateral branches below the first truss, on widely spaced plants, of the variety 'Potentate' gave a yield nearly three times as great as on single-stemmed plants. It was of importance to discover whether this constituted an increase in yield per unit area of glasshouse space, the factor of most concern to the grower. This has been investigated in preliminary experiments by comparing the yields from plants having no side shoots and plants in which side shoots below the first truss had been allowed to develop. Three differen spacings between the rows were used. The greatest yield per unit area was obtained from single-stemmed plants at the two closest spacings, namely, 2 ft. and 3 ft., although multistemmed plants at 3 ft. and 4 ft. spacings had the greatest mean weight of individual fruit. No treatment had any effect on weight per unit area of early fruit.

A review of the literature on spacing of tomato plants in commercial cultivation, included in the report, shows that there is no simple answer to the question of optimal planting density for maximum yield. It is thought that this may be because insufficient attention has been given to possible interactions between planting density and watering and manuring. The study of the composition of the tomato fruit has been continued by the Chemistry Department, especially in relation to variety and state of ripeness of the fruit, with special reference to fruit quality and ripening disorders. It was concluded that the latter, evident by their effects on the outer fruit wall, were also related to the composition of the inner portion of the fruit. Further investigations were made of the changes during ripening. The acidity in the wall increased from the green stage to the first appearance of yellow pigmentation, but there was no consistent trend as ripening proceeded. This was in contrast to the situation in the inner portion of the fruit, where acidity decreased and sugars (mainly glucose and fructose) increased. The concentration of soluble solids in the expressed sap of the tomato varies considerably in relation to fruit quality and variety. These investigations will be facilitated by the demonstration that measurement of refractive index by a simple hand refractometer gives a reliable indication of total dissolved solids.

Work on urea–formaldehyde compounds as slow-acting nitrogenous fertilizers has been concluded, and a report gives the relative merits of the several compounds tested. Liquid feeding of tomatoes is of considerable topical interest, especially in connexion with automatic irrigation, and research on this problem has been resumed. Magnesium deficiency

* Glasshouse Crops Research Institute. Annual Report 1957. Pp. 161. (Littlehampton: Glasshouse Crops Research Institute, 1958.) 10s.

in glasshouse tomatoes is common, and preliminary results indicate that foliar sprays containing magnesium are more effective than soil treatments in maintaining normal leaf colour. The plant-breeding programme is concerned mainly with improvements of tomato, cucumber and lettuce.

The investigations on *Didymella* stem rot of tomato have been continued by the Plant Pathology Department, which is also concerned with powdery mildew of cucumber and wilt disease of carnation as well as mushroom diseases. Some experiments were carried out on chemotherapeutic control of tobacco mosaic virus in the tomato, but it was concluded that this approach is not promising. Although insecticides properly applied should give adequate control of white fly, there are sometimes risks of chemical injury to plants, and for this reason interest has been revived in the method of biological control by wasp parasites. The Entomology Department has begun a series of studies on the effects of environmental factors on the fecundity and development of white fly and on the host/parasite balance. Other investigations by this Department include mushroom pests and the red spider mite. The Crop Protection Department is concerned with the control of mildew of chrysanthemums and aphids on lettuce and with the residual toxicity of certain sprays.

E. C. Humphries

RADIOLOGICAL HAZARDS TO PATIENTS

At the end of 1956, the Secretary of State for Scotland and the Minister of Health appointed a committee "to review the present practice in diagnostic radiology and the use of radiotherapy in non-malignant conditions, having regard to the report of the Committee on the Hazards to Man of Nuclear and Allied Radiations".

This committee, under the chairmanship of Lord Adrian, has now produced an interim report (Ministry of Health; Department of Health for Scotland. Radiological Hazards to Patients: Interim Report of the Committee. Pp. 22. London: H.M. Stationery Office, 1959. 1*s*. 3*d*. net) for the one completed part of its survey, namely, the use of X-rays for mass miniature radiography. The conclusion is drawn that, when properly conducted, examinations by this method make a negligible contribution to the total radiation to which the population is daily exposed. Even on the most pessimistic assumptions, the indefinite continuation of mass miniature radiography at the present rate could add no more than 20 cases of leukæmia to the annual incidence of 2,500 cases in Great Britain; it is also possible that it would produce no additional cases at all. The gonad doses, which determine the long-range genetical damage, have been found to be even smaller than previously estimated. These very small somatic and genetical risks have to be considered in relation to the undoubtedly large benefits of mass miniature radiography to the health of the population. In 1957, these examinations led to the discovery of nearly 18,000 cases of pulmonary tuberculosis and some 63,000 other abnormalities, which included lung cancer, heart disease and pneumoconiosis. For children and pregnant women, mass miniature radiography is not recommended and should be replaced by normal radiographic procedures with strict limitation of the field to the chest. Some general principles are also given for reducing unnecessary exposure in other forms of diagnostic radiology, in particular fluoroscopy; but the survey of this area is not yet completed.

There is one statement in the introduction (paragraph 10) which may give rise to serious misunderstandings. It is stated, correctly, that a dose of radiation which would double the present mutation-rate would cause perceptible damage to the population, and that this dose is estimated to lie between 10 and 100 r. per generation. It is also correct to say that at present the dose due to medical radiology does not exceed 3 rads per generation. But it is only for the sake of convenience that genetical damage is usually estimated in terms of the 'doubling dose'. There is no lower threshold to the genetical effects of ionizing radiation, and serious genetical damage will be produced already by doses which are far below the doubling dose. In fact, the report of the Medical Research Council came to the conclusion that, from the point of view of genetical hazards, "the upper limit, which future knowledge may set to the total dose of extra radiation which may be received by the population as a whole, is not likely to be more than twice the dose which is already received from the natural background; the recommended figure may indeed be appreciably lower than this". On this evidence, the danger limit has already been reached or even exceeded in countries where X-rays are used extensively for medical purposes. Against this damage to future generations we must, however, set the benefit to the present one and, although all means must be used to cut down avoidable exposure to radiation, a high amount of exposure will remain unavoidable if the present standards of medical service are to be maintained.

FEEDING THE HUNGRY

The practical way to wage war on want was the theme of an outstanding address at St. John's College, Annapolis, Maryland, on April 9 by Mr. Gerard Piel, publisher of *The Scientific American*. Following an account of the way in which science has given man unlimited power and opportunities to change the material conditions of life, Piel shows how it is now possible to bring the elimination of want within the reach not only of the present generation but also of all future generations. Want is no longer a challenge to technology, but to economics and politics; it is a social problem. Thanks principally to the control of mortality, the underprivileged peoples are living longer and feeling well enough to do something about their plight. These aroused people are still extracting the irreplaceable resources of their lands to feed the voracious appetite for raw materials of Western peoples. At present the

United States imports from overseas iron ore, bauxite, oil and a host of commodities in greater volume than ever before. In some American sectors the technology is perilously dependent upon riches supplied so cheaply. The goodwill and compliance of the natives have immediate relevance to the American price structure.

It is impossible to stop at the churlish counsel that the Colonials should reduce their numbers. Their population is rising because the modicum of sanitation introduced to protect white Colonials in their midst has reduced their rate of mortality as well. Their numbers are increasing, according to United Nations studies, at a rate that exceeds 1 per cent per annum. Since the end of the Second World War their material condition has been in corresponding decline; their calorie intake has actually fallen.

To offset the claim of population growth and reverse the decline in their condition, they must increase their production at a rate greater than their population growth. The larger the differential, the faster will their lot improve. Such an objective is not only technologically but also politically and economically feasible. American industrial growth has averaged 5 per cent over long periods; it has reached 8 per cent under intense pressure. The growth of agricultural output has correspondingly proceeded at the rate of 2 per cent in normal times. In response to the economic cycle and to controlled prices and other regulatory devices, it fluctuates over an even wider range. The present curtailment of grain production in the United States represents 200,000 tons, which approximates to the calorie deficit for the underfed portion of the world population.

About 500 billion dollars over the next fifty years would secure an average gain per annum of 2 per cent in industrial production and a corresponding increase in agricultural output in non-Western areas. Not all the 500 billion dollars would have to be supplied from outside. At about the halfway point the new industrial centres would begin to generate some additional capacity of their own.

Bed-rock investments, however, are not particularly attractive to the world's capital market. These involve such elementary public utilities as communication systems, including highways as well as railroads, and dams for flood control and irrigation. Investments in such projects call for the kind of funds now written off on armaments. A long-range view should be taken in looking for return on investment.

Western technology is specially qualified to contribute to the soaring demand for electrical energy which will attend industrialization programmes. But the demand for huge volumes of energy, heavy equipment and big investment would not come at the outset. First, there is need for planning and, then, engineering. Many of the early gains in these areas would be achieved with very little expenditure on capital goods. The first requirement is for brains and knowledge.

An example of what can be accomplished is furnished by Mexico. For the past twenty years the Rockefeller Foundation has been working with the Ministry of Agriculture and Animal Husbandry of Mexico. At a cost of less than 2 million dollars a year, American agronomists have been supplied to Mexico, and young Mexicans have been trained in the agricultural sciences. In this period, the food production of the country has risen 80 per cent. The gains have been achieved by improved yields of Mexico's own staple crops, the development of new varieties of wheat and potatoes and the establishment of something like the American county-agent system for farmer education. Not a single tractor or fertilizer plant is in the expense account; the money has been spent on the intangibles of information, education and expert consultation. The 4 per cent per annum gain safely exceeds the 3 per cent increase in population and has brought an improvement in the people's diet which is already showing up in vital statistics.

Somewhere in American material and intellectual resources the capacity to expand on this precedent could be found. If a beginning could be made, it would soon be possible to have additional wealth and brains available for the task as a result of the attenuation of the arms race on which prosperity now rests so heavily and insecurely.

SYMPATHETIC POSTGANGLIONIC MECHANISM

By Prof. J. H. BURN, F.R.S., and M. J. RAND
Department of Pharmacology, University of Oxford

DURING recent years it has been demonstrated that acetylcholine exerts an action in various organs similar to that of sympathetic stimulation. Since this action is seen in the presence of atropine and is also exerted by nicotine, it follows that the action is not a muscarinic but is a nicotinic action. An example of this action is the contraction of the arrectores pili muscles in the skin of the cat's tail. This was first described by Brücke[1] for acetylcholine, and a few years later by Coon and Rothman[2] for nicotine. Most of the hair was removed from the cat's tail except for a few tufts, and acetylcholine or nicotine was injected into the skin at the base of the tufts. Pilo-erection was then observed. Normally the pilomotor muscles are caused to contract by sympathetic stimulation, and they also contract after the intravenous injection of adrenaline or noradrenaline. Other examples of sympathomimetic effects caused by acetylcholine or by nicotine in the presence of atropine are the relaxation of the isolated intestine of the kitten by nicotine[3]; the acceleration of the isolated atria of the rabbit[4] and the constriction of the vessels of the perfused rabbit ear by acetylcholine and by nicotine[5]; the contraction of the isolated nictitating membrane of the cat by nicotine[6]. de Burgh Daly and Scott (unpublished work) have observed that acetylcholine injected into the splenic artery during perfusion of the spleen with blood caused contraction of the spleen. We are grateful to them for allowing us to quote this result.

These nicotine-like effects of acetylcholine, exerted at sites peripheral to sympathetic ganglia, thus

resemble the effects of sympathetic stimulation; they are not seen in preparations from animals treated with reserpine. Tissues innervated by sympathetic nerves were found by Schmiterlöw[7] and by Euler and Purkhold[8] to contain noradrenaline together with a much smaller amount of adrenaline. After treatment of rabbits with reserpine, the noradrenaline which can be extracted from the heart disappears[9]. Similarly after treatment with reserpine, the noradrenaline disappears from the aorta of the dog and of the rabbit, from the skin of the rabbit's ear and from the skin of the cat's tail, from the cat's spleen and from the iris of the cat's eye[10].

The nicotine-like actions of acetylcholine are also lost when the sympathetic fibres degenerate, and this degeneration is also accompanied by a loss of the noradrenaline which can be extracted from the organ[8,10b].

The conclusion may therefore be drawn that the nicotine-like actions of acetylcholine which have been described are due to the release of noradrenaline (possibly with adrenaline also) from the organ.

At present we are uncertain of the location of the noradrenaline in the organ. v. Euler[11] believes that it is contained within the postganglionic fibres, calculating that the amount may be 3–30 mgm./gm. This is one thousand times more than that in postganglionic fibres before they reach the organ. This amount is only of the order of 15 μgm./gm. The disappearance of the noradrenaline after degeneration of the nerves is readily explained if it is present in the nerves.

There is some evidence, which as yet is only suggestive, that the noradrenaline and adrenaline in the organs might be present in cells containing chromaffin granules. Such cells have been described in human skin by Adams-Ray and Nordenstam[12], and also by Burch and Phillips[13]. They have been found in the skin of the rabbit's ear, in the skin of the cat's tail and in the nictitating membrane. The chromaffin granules are greatly reduced or disappear in the tissues of animals treated with reserpine, or in tissues in which the sympathetic fibres have degenerated[10d,e]. Thus it is possible that the nicotine-like actions of acetylcholine are due to the release of noradrenaline and adrenaline from cells containing chromaffin granules. However, Muscholl and Vogt[14] have found that reserpine depletes the noradrenaline stores in the sympathetic neurones more readily than those in chromaffin cells.

Tyramine is a sympathomimetic amine which ceases to act after degeneration of the sympathetic fibres[15]. Its pressor action is also absent in the cat previously treated with reserpine[16]. The conclusion may be drawn that tyramine exerts its action by liberating noradrenaline and adrenaline from the store in the organ. Since an infusion of noradrenaline into the vein of a cat or into the blood perfusing the hind-leg of a dog increases the pressor and constrictor action of tyramine, or restores it when it is absent due to previous treatment with reserpine, it appears that the store of noradrenaline in the organ can be increased by taking up noradrenaline from the blood stream[17].

The effect of sympathetic stimulation also is increased as a result of an infusion of noradrenaline. If the volume of one hind-leg of a dog is recorded in experiments in which the lumbar sympathetic chain is stimulated, then, atropine having been given, the threshold strength of stimulus for causing vasoconstriction in the hind-leg can be determined. Following an infusion of noradrenaline, the total amount given to the dog being 0·2–1·0 mgm. in the course of 20 min., the threshold has been observed to fall to a mean of 40 per cent of its previous value. In experiments in which the dog's hind-leg has been perfused it has been observed that the effect of a given sympathetic stimulus was greatly increased. These observations indicate that the efficiency of sympathetic stimulation depends on the amount of noradrenaline in the neighbourhood of the nerve endings. This may be taken up from the blood into the nerve endings themselves or into chromaffin cells; one of the functions of the noradrenaline secreted by the adrenal medulla may be to fill up this store.

We have now considered evidence that the nicotine-like actions of acetylcholine are due to the release of noradrenaline from a store near the sympathetic nerve endings; we have seen that this store can take up noradrenaline which is circulating in the blood, and we have seen that the effect of sympathetic stimulation depends on the size of this store. We now turn to the sympathetic impulses themselves.

When a cat is treated with reserpine with the result that the stores of noradrenaline and of adrenaline are depleted, the effect of tyramine on the nictitating membrane is completely absent, but stimulation of the postganglionic sympathetic fibres still causes a contraction. The threshold strength for this effect is greater than the threshold in the normal cat. We have found that the contraction produced is augmented by eserine and is abolished by atropine, and the contraction must therefore be due to the release of acetylcholine from the sympathetic fibres. The presence of cholinergic fibres in the sympathetic supply to the nictitating membrane was suggested by Bacq and Fredericq[18]. Recent work shows that the presence of cholinergic fibres is still more widespread. Thus Gillespie and Mackenna[19] have found that when a rabbit is treated with reserpine, the isolated colon is caused to contract by sympathetic stimulation instead of to relax, and that the contraction is abolished by atropine. They concluded that cholinergic fibres are present in the sympathetic supply.

Huković[20], working in this Department, has made an isolated preparation of rabbit atria with the sympathetic nerves attached; when the sympathetic fibres from the stellate ganglion were stimulated the rate and amplitude of the atrial beat increased. If the rabbit was treated beforehand with reserpine some preparations responded to sympathetic stimulation by inhibition, the inhibitor effect being increased by eserine and abolished by atropine. This result suggests that cholinergic fibres are present in the sympathetic supply from the stellate ganglion to the atria.

Observations have also been made on the cat spleen, recording the changes in volume of the spleen by a plethysmograph. The nerves were separated from the splenic artery near the beginning of the artery. Stimulation caused contraction of the spleen which was unaffected by atropine. When the cat was treated beforehand with reserpine, it was found that in some preparations acetylcholine caused a dilatation of the spleen, and that stimulation of the nerves was also followed by dilatation. This dilatation was increased in the presence of eserine and abolished by atropine. Thus the splenic nerves also contain cholinergic fibres. Observations have also been made on the

virgin cat uterus, recording its contractions *in situ* under chloralose anæsthesia. When the hypogastric nerves were stimulated, inhibition followed. When the cat was treated beforehand with reserpine, stimulation of the hypogastric nerves caused a small contraction which was greater in the presence of eserine and which was abolished by atropine. The evidence suggests that the hypogastric nerves contain cholinergic fibres.

The observations that the nicotine-like effects of acetylcholine resemble those of sympathetic stimulation, and that these effects are exerted by the release of noradrenaline (or adrenaline), must now be put side by side with the evidence of the existence of cholinergic fibres in postganglionic sympathetic fibres in various places where they were not suspected. It then appears that such cholinergic fibres may be adrenergic in their effect, because the acetylcholine which they liberate will cause the discharge of noradrenaline or of adrenaline from the peripheral store. The stimulation of such fibres can in theory have two effects, one, normally much the smaller, due to the direct action of the acetylcholine released, an action which is sensitive to atropine, and the other, normally much the greater, due to the released acetylcholine causing a discharge of noradrenaline from the store, a nicotine-like action not affected by atropine. This double effect may actually be present in the nictitating membrane, where the response to postganglionic stimulation in the normal cat is slightly diminished by atropine, for example to about 80 per cent of its initial size.

Such a double effect might explain the response to stimulation of the sympathetic supply to the muscles of the dog's hind-leg, where Burn[15b] observed that a stimulus for 3 sec. caused dilatation, while the same stimulus applied for 30 sec. caused in the main constriction. A double effect is possible only when acetylcholine has a direct muscarinic action of its own. Thus in the cat treated with reserpine, stimulation of the sympathetic fibres has no pilomotor effect in the tail. The accumulated evidence thus requires consideration of a new possibility. The adrenergic sympathetic fibre has been thought of as liberating noradrenaline in the same way as cholinergic fibres liberate acetylcholine. However, cholinergic fibres, which seem widespread in the postganglionic sympathetic supply, may liberate noradrenaline from the store at the nerve endings, and thus be adrenergic in effect.

In this account we have kept open the possibility that noradrenaline may not always be the main component of the peripheral store and that around some sympathetic nerve endings, in the virgin cat uterus, for example, adrenaline may be more important. We have no evidence on this as yet. We may also recall that Pines[21] has described the chromaffin cells in sympathetic ganglia and has given a detailed account of his findings that they are innervated.

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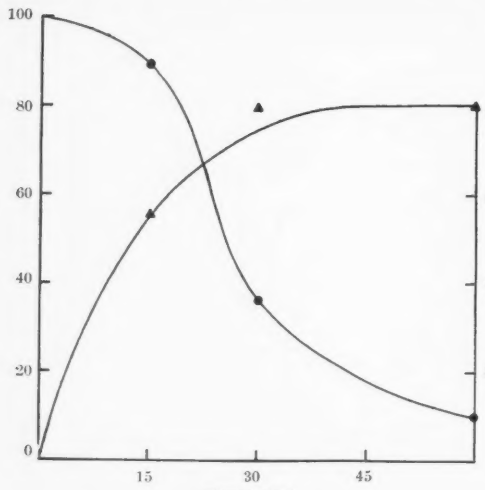
PROTEIN BIOSYNTHESIS AND OXIDATIVE PHOSPHORYLATION IN ISOLATED RAT LIVER MITOCHONDRIA

By P. J. REIS, J. L. COOTE and T. S. WORK

National Institute for Medical Research, Mill Hill, London, N.W.7

ELECTRON microscopy combined with differential centrifugation of sucrose homogenates has shown that liver parenchymal cells have a complex cytoplasmic structure[1]. After intravenous injection of amino-acids labelled with carbon-14 the proteins of the subcellular cytoplasmic structures of these cells become labelled at different rates. In both rats and guinea pigs the liver microsomal fraction is labelled considerably more rapidly than the mitochondrial material. Labelling is particularly rapid in the ribonucleoprotein fraction of the microsomes[2]. The suggestion has been made that protein synthesis takes place mainly in the microsomal ribonucleoprotein fraction and that mitochondria acquire radioactive protein from the microsomal fraction. The present results and those of Bates *et al.*[3] indicate that rat liver mitochondria are capable of independent protein synthesis.

Mitochondria were isolated from rat liver by differential centrifugation of a 1 : 4 sucrose homogenate. Best results were obtained with a mixture containing sucrose (0·3 *M*), versene (0·002 *M*) and nicotinamide (0·03 *M*); this mixture will be referred to as SVN. The fraction collected between 1,000 and 6,000*g* was washed by four successive cycles of re-suspension in and precipitation from SVN. Washed mitochondria in a mixture of sucrose (0·15 *M*), phosphate (0·01 *M*), tris buffer (0·02 *M*), $MgSO_4$ (0·008 *M*) and sufficient KCl to maintain tonicity showed negligible incorporation of labelled amino-acids into mitochondrial protein during aerobic incubations. The mitochondrial protein was obtained by precipitation with trichloroacetic acid and treatment to remove adsorbed amino-acids, ribonucleic acid and lipids. Incorporation was stimulated by the addition of either succinate or α-ketoglutarate,



Ordinates: left, per cent of initial rate of oxidative phosphorylation; right, counts per min.

Fig. 1. Dependence of incorporation of amino-acid into mitochondrial protein upon oxidative phosphorylation. Washed mitochondria from about 3 gm. rat liver were suspended in 5·5 ml. of medium of the following composition: *tris* buffer (0·05 *M*), potassium phosphate (0·01 *M*), potassium succinate (0·01 *M*), magnesium sulphate (0·008 *M*), potassium chloride (0·065 *M*), versene (0·0013 *M*), nicotinamide (0·02 *M*), ^{14}C-*Chlorella* protein hydrolysate (5 μc.), sucrose (0·11 *M*), added as 2·0 ml. boiled cell sap. Incubations were at 30°, in an atmosphere of oxygen. Oxidative phosphorylation was measured essentially as described by Slater (ref. 10); glucose-6-phosphate was estimated by the method of Kornberg and Horecker (ref. 11)

together with cell sap. At an early stage in the investigation it was found that, contrary to the report of Greengard[4], boiled cell sap was just as effective as whole cell sap. Both the rate and the duration of amino-acid incorporation into mitochondrial protein could be increased by adding progressively larger quantities of boiled cell sap. The incorporation reaction was stimulated by incubation in oxygen instead of air and almost completely inhibited by incubation in nitrogen or by the addition of dinitrophenol or cyanide. The behaviour of the incorporation reaction towards inhibitors indicated that incorporation was probably linked to oxidative phosphorylation; amino-acid incorporation and oxidative phosphorylation were accordingly measured in the same mitochondrial preparation. The results (Fig. 1) showed that as the rate of oxidative phosphorylation declined, the rate of incorporation declined in a similar manner.

The duration of oxidative phosphorylation in isolated rat liver mitochondria is notoriously sensitive to conditions of incubation[5]. Calculation of the amount of adenine nucleotide in boiled cell sap indicated that the final concentration of nucleotides in the incubation mixture was below that usually required to maintain mitochondrial structure and oxidative phosphorylation. Accordingly, the boiled cell sap was supplemented with 0·004 *M* adenosine monophosphate and 0·0005 *M* diphosphopyridine nucleotide. Mitochondria incubated under these conditions were able to maintain oxidative phosphorylation and incorporation of labelled amino-acids for 2 hr. at 30°, although the rate of incorporation was falling off after 1 hr. The work of Siekevitz and Potter[5] and of Pressman[6] indicates that the balance of nucleotides and of inorganic phosphate inside the mitochondrial membrane is best maintained when an acceptor for energy-rich phosphate bonds is present in the medium. Thus when the system was further supplemented with hexokinase and glucose, incorporation of amino-acids into mitochondrial protein could be maintained at, or near, a linear rate for 2 hr. at 30°. Incubations have not been carried beyond 2 hr.

Mitochondria are composed of a structurally complex double membrane within which are disposed various soluble but rather firmly bound enzymes. It was found that in the presence of adenosine monophosphate and diphosphopyridine nucleotide, both with and without hexokinase, the insoluble proteins of the mitochondria were effectively labelled either by a mixture of amino-acids labelled with carbon-14 or by a single labelled amino-acid (phenylalanine). Soluble protein was not, however, significantly labelled even after 2 hr. at 30° (soluble protein was released either by the butanol method of Morton[7] or by the extraction of an acetone-dried powder of mitochondria with phosphate buffer). Increase in the amount of boiled cell sap, with maintenance of the adenosine monophosphate and diphosphopyridine nucleotide concentration at the level given above, resulted in a substantial improvement in the efficiency of labelling of the insoluble protein and produced slight activity in the soluble protein. Boiled cell sap contains substantial quantities of amino-acids (80 μgm. amino-nitrogen/ml.) and it was found that these could be replaced by a complete mixture of 20 amino-acids. It was found that, as the concentration of these amino-acids in the incubation medium was progressively increased, the incorporation into insoluble protein rose to a maximum at an amino-acid concentration of 30–40 μM/ml. The incorporation into soluble protein was initially low; but as amino-acid concentration was increased, the radioactivity of the soluble protein continued to rise in an approximately linear manner. Thus the incorporation into soluble protein of the mitochondria progressively becomes a greater proportion of the total incorporation, as amino-acid concentration is increased. The most likely explanation of these results is that there are relatively few sites of protein synthesis in mitochondria (templates ?). When these sites become saturated with incoming radioactive amino-acid further increase in amino-acid concentration (of fixed specific radioactivity) will not result in any further increase in radioactivity of insoluble protein. Increased amino-acid concentration will result, however, in a progressively greater tendency for newly synthesized protein to be displaced from the sites of synthesis into the intracisternal spaces so that there will continue to be a progressive increase in the rate of accumulation of radioactivity in soluble protein.

There is no doubt that the amino-acid incorporation reaction measured in these experiments is truly intramitochondrial and is not due to adherent microsomes. First, incorporation is not abolished by thorough washing of the mitochondria as described previously (this washing procedure has been shown to remove at least 95 per cent of microsomes labelled with carbon-14 added to the sedimented mitochondria); secondly, the incorporation reaction does not require fresh cell sap with its supply of soluble ribonucleic acid[8] and 'amino-acid activating' enzymes; thirdly, the incorporation is much more prolonged than that obtained with microsomes *in vitro*; and fourthly, the incorporation is quite unaffected by addition of ribonuclease to

the incubation mixture. This does not, however, prove that ribonucleic acid plays no part in amino-acid incorporation since we have found that, even after 2 hr. at 30° in the presence of ribonuclease, mitochondria retain about 70 per cent of their ribonucleic acid (originally 17 μgm./mgm. mitochondrial protein). Indeed, the incorporation reaction in mitochondria may have closely similar characteristics to that occurring in microsomes since we have found that an extract of mitochondria will catalyse an amino-acid-dependent exchange between adenosine triphosphate and radioactive pyrophosphate (Table 1).

Table 1. AMINO-ACID ACTIVATION IN RAT LIVER MITOCHONDRIA

Extract of mitochondria prepared from :	c.p.m. per μmole adenosine triphosphate		
	No amino-acids	Plus amino-acids	Increment due to amino-acids
0·6 gm. Liver	1,810	2,400	580
1·2 gm. Liver	3,060	4,280	1,220

Mitochondria were isolated and washed four times; an acetone powder was prepared and extracted with 0·1 *M* tris buffer, *p*H 7·6. This soluble extract was incubated with: tris buffer, *p*H 7·6, 100 μmoles; magnesium chloride, 2 μmoles; adenosine triphosphate, 5 μmoles; a mixture of 12 amino-acids, 2 μmoles of each; ^{32}P-pyrophosphate, about 2 μmoles, 150,000 c.p.m.; vol. 1 ml. Incubated for 15 min., 37°.

Before one can be convinced that the amino-acid incorporation observed in these experiments represents true synthesis of protein, it would be necessary to demonstrate synthesis of a specific protein. In this regard the synthesis of cytochrome *c* has already been demonstrated in isolated mitochondria from rat liver[8] and calf heart[9]. The presence of numerous enzymes within mitochondria suggests that this *in vitro* system should be a valuable tool in further studies on protein biosynthesis. Work has already been initiated along these lines.

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STRUCTURE OF A MELANOCYTE-STIMULATING HORMONE FROM THE HUMAN PITUITARY GLAND

By DR. J. IEUAN HARRIS*

Department of Biochemistry, University of Cambridge, and the Biological Laboratories, Harvard University

A MELANOCYTE-STIMULATING substance from human pituitary glands has recently been isolated in pure form by ion-exchange chromatography[1]. It has been shown to be a slightly basic polypeptide which migrates as a single substance when submitted to ionophoresis on paper in pyridine-acetic acid buffers at *p*H's of 3·6 and 6·5.

The amino-acid sequence of the polypeptide hormone has been investigated by methods similar to those described[2,3] for the elucidation of the structure of α-melanocyte-stimulating hormone from pig pituitary glands. The particular methods which have been used were to a great extent determined by the limited amount of the substance (4–5 mgm.) which was available for study.

Specific colour tests[4] carried out on the intact polypeptide showed that it contained tryptophan, tyrosine, histidine and arginine; and when a total acid hydrolysate was submitted to qualitative chromatographic analysis on paper the following amino-acids were shown to be present: alanine, arginine, aspartic acid, glutamic acid, glycine, histidine, lysine, methionine, phenylalanine, proline, serine, and tyrosine.

A sample of the hormone (2·5 mgm.) was allowed to react with chymotrypsin (0·1 mgm.) in 0·05 *M* ammonium bicarbonate (2 ml.) at *p*H 8·0–8·5 and 37° for 10 hr. When the product was fractionated by ionophoresis on paper in pyridine-acetic acid (*p*H 6·5) at 40 volts/cm. for 2 hr. it was resolved into five peptide fragments.

* Member of the Scientific Staff of the Medical Research Council (at present Research Fellow in Biology, Harvard University, Cambridge, Mass.)

Table 1. AMINO-ACID COMPOSITION AND C-TERMINAL AMINO-ACIDS OF PEPTIDES PRODUCED BY CHYMOTRYPTIC HYDROLYSIS OF HUMAN β-MELANOCYTE-STIMULATING HORMONE

Peptide	Amino-acid composition	C-terminal group
C_1	Ala,Asp,Glu,Gly,Lys,Pro,Tyr	Tyr
C_2	Arg,Asp,Gly,Lys,Pro,Ser,Try	Asp
C_3	Arg,Glu,His,Met,Phe	Phe
C_5	Asp,Gly,Lys,Pro,Ser	Asp
C_6	Arg,Try	Try

The amino-acid compositions of these five peptides (C_1, C_2, C_3, C_5 and C_6) were determined by means of specific colour tests[4], and by paper chromatographic analysis of their total acid hydrolysates; the corresponding C-terminal amino-acids were determined by means of carboxypeptidase[5]. The results, summarized in Table 1, showed that the human melanocyte-stimulating hormone was of the 'β-melanocyte-stimulating hormone' type, and that it was closely related in terms of chemical structure to β-melanocyte-stimulating hormone[6,7] from pig pituitary glands. Thus, peptides C_2, C_3, C_5 and C_6 were found to have the same electrophoretic mobilities at *p*H 3·5 and *p*H 6·5, and the same qualitative amino-acid compositions (with the exception of C_3, which contained arginine instead of lysine), as the corresponding peptide fragments[6] derived from pig β-melanocyte-stimulating hormone by digestion with chymotrypsin. Peptide C_1, on the other hand, differed from the corresponding peptide fragment from pig β-melanocyte-stimulating hormone, both in electrophoretic and chromatographic behaviour, and in amino-acid composition, although the C-terminal amino-acid,

tyrosine, and four of the other constituent amino-acids—aspartic acid, glutamic acid, glycine and proline—were common to both peptide fragments.

The presence of lysine suggested that C_1 would be susceptible to the action of trypsin. It was therefore allowed to react with trypsin for 4 hr. at 37°; when the product of reaction was fractionated by ionophoresis at *p*H 6·5 it was resolved into two major (C_1TA_1, C_1TB_1) and two minor (C_1TA_2, C_1TB_2) components. Their qualitative amino-acid compositions were determined and are given in Table 2.

Table 2. Amino-acid Composition and C-terminal Amino-acids of Peptides produced by Tryptic Hydrolysis of Peptide C_1 (Table 1)

Peptide	Amino-acid composition	C-terminal group
C_1: TA_1	Asp,Glu,Gly,Lys,Pro,Tyr	Tyr
TB_1	Ala,Glu,Lys	Lys
TA_2	Asp,Glu,Gly,Pro,Tyr	Tyr
TB_2	Lys	—

One of the minor peptide components, C_1TA_2, appeared to be identical with the N-terminal peptide, Asp.Glu.Gly.Pro.Tyr., in pig β-melanocyte-stimulating hormone[6], as judged by its electrophoretic mobility at *p*H 6·5, R_F in butanol-acetic acid-water (4 : 1 : 5), amino-acid composition, and C-terminal group. The two major peptide components, C_1TA_1 and C_1TB_1, were both found to contain lysine; and the fact that a significant amount of free lysine (C_1TB_2) was also formed in the tryptic reaction suggested that the parent molecule, C_1, contained a Lys.Lys bond, and that it was the N-terminal peptide (Ala, Glu.).Lys.Lys.(Asp.Glu.Gly.Pro).Tyr in the human β-melanocyte-stimulating hormone molecule.

After their homogeneity had been established both by electrophoretic and chromatographic analysis, peptides TA_1, TA_2, TB_1 and C_3 were submitted to partial acid hydrolysis (12 *N* hydrochloric acid, for 3–6 days at 37°); peptide C_2 was hydrolysed with subtilisin[8] (12 hr. at 37°). The respective products of reaction were fractionated by ionophoresis on paper and were characterized by the procedures which have been described previously[3,6]. The results are summarized in Table 3.

Peptide C_2 was shown to give additional amounts of C_5 and C_6 when it was redigested with chymotrypsin, showing that C_5 and C_6 formed contiguous sequences in the molecule. By means of carboxypeptidase, C_6 was shown to be a dipeptide containing arginine and tryptophan; in a similar manner aspartic acid was shown to be the C-terminal amino-acid in both C_2 and C_5, showing that these two peptides formed the C-terminal sequence, Arg.Try.(Gly,Ser,Pro,Lys).Asp, in human β-melanocyte-stimulating hormone (cf. ref. 6).

Although it was not found possible to undertake quantitative amino-acid and end-group analyses on the parent molecule, the results which have been

Table 3. Peptides Identified in Partial Acid* (12 *N* Hydrochloric Acid, 37°) and Subtilisin† Hydrolysates

Peptide	Products of partial hydrolysis
*C_1TB_1	Ala.Glu, Glu.Lys
*C_1TA_1	Lys.Asp, Lys.Asp.Glu, Glu.Gly, Gly.Pro.Tyr
*C_5	Ser.Pro, Ser.Pro.Pro, Ser.Pro.Pro.Lys, Pro.Pro.Lys, Pro.Lys, Lys.Asp.
†C_6	Arg.Met, Arg.Met.Glu, Glu.His, Glu.His.Phe.

obtained with peptide fragments derived from it by hydrolysis with chymotrypsin and trypsin nevertheless appear to be sufficient to establish that human β-melanocyte-stimulating hormone contains twenty-two amino-acid residues, and that they occur in the following sequence:

1 2 3 4 5 6 7 8 9 10 11
H— Ala.Glu.Lys.Lys.Asp.Glu.Gly.Pro.Tyr.Arg. Met.
12 13 14 15 16 17 18 19 20 21 22
Glu.His.Phe.Arg.Try.Gly.Ser.Pro.Pro.Lys.Asp. — OH

This appears to be the first of the polypeptide hormones from the human pituitary to be isolated in pure form and to be characterized in terms of its complete chemical structure. The amino-acid sequences of human, pig[6,7] and ox[9] β-melanocyte-stimulating hormones and pig α-melanocyte-stimulating hormone[2,3] are compared in Fig. 1.

Although human β-melanocyte-stimulating hormone manifests a structural 'species' difference of the 'classical' type, namely, the replacement of a lysine residue (position 6 in pig and ox β-melanocyte-stimulating hormone) by arginine (position 10 in human β-melanocyte-stimulating hormone) in structurally related positions, the presence of the additional N-terminal tetrapeptide, Ala.Glu.Lys.Lys, represents a hitherto unprecedented structural species variation among naturally occurring biologically active polypeptide and protein molecules of relatively low molecular weight (for example, vasopressins[10,11], corticotropins[12], insulins[13] and hypertensins[14,15]).

Ox β-melanocyte-stimulating hormone[9] is found to differ from pig β-melanocyte-stimulating hormone only in position 2 (Fig. 1), where the glutamic acid residue in the pig hormone is replaced by a serine residue in the ox hormone. It is perhaps significant that the replacement of one amino-acid by another which is structurally unrelated to it occurs in a part of the molecule which does not appear to be specifically essential for its biological activity[3] (cf. corticotropins[12]). Presumably genetical alterations which produce structural modifications of this type in essential parts of the molecule would result in the formation of molecules in which biological specificity was either modified or destroyed. Consequently the fact that a lysine residue in the pig and ox hormones is replaced by the structurally related amino-acid, arginine, in the human hormone, and that the structural features common to all known β-melanocyte-stimulating hormones and corticotropins[12,16]

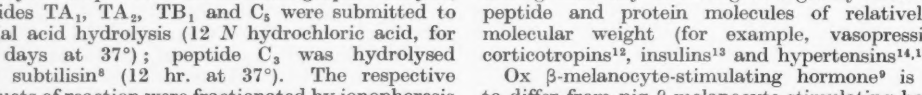
α-MSH (pig)
1 CH3CO-Ser. 2 Tyr. 3 Ser. 4 Met. 5 Glu. 6 His. 7 Phe. 8 Arg. 9 Try. 10 Gly. 11 Lys. 12 Pro. 13 Val—NH2
β-MSH (ox)
H— 1 Asp. 2 Ser. 3 Gly. 4 Pro. 5 Tyr. 6 Lys. 7 Met. 8 Glu. 9 His. 10 Phe. 11 Arg. 12 Try. 13 Gly. 14 Ser. 15 Pro. 16 Pro. 17 Lys. 18 Asp. —OH
β-MSH (pig)
H— 1 Asp. 2 Glu. 3 Gly. 4 Pro. 5 Tyr. 6 Lys. 7 Met. 8 Glu. 9 His. 10 Phe. 11 Arg. 12 Try. 13 Gly. 14 Ser. 15 Pro. 16 Pro. 17 Lys. 18 Asp. —OH
β-MSH (human)
H— 1 Ala. 2 Glu. 3 Lys. 4 Lys. 5 Asp. 6 Glu. 7 Gly. 8 Pro. 9 Tyr. 10 Arg. 11 Met. 12 Glu. 13 His. 14 Phe. 15 Arg. 16 Try. 17 Gly. 18 Ser. 19 Pro. 20 Pro. 21 Lys. 22 Asp. —OH

Fig. 1. Amino-acid sequences of melanocyte-stimulating hormones from pig, ox and human pituitary glands. MSH, melanocyte-stimulating hormone

remain intact, suggests that the amino-acids which occupy these key positions in β-melanocyte-stimulating hormone are directly associated with its biological activity in the *in vivo* environment in which it has been designed to function as a hormone.

In α-melanocyte-stimulating hormone, on the other hand, there is an *interchange* of lysine and serine residues between positions 3 and 11 (Fig. 1), which correspond to positions 6 and 14 in pig and ox β-melanocyte-stimulating hormones, and to positions 10 and 18 in human β-melanocyte-stimulating hormone. This would suggest that factors other than the linear arrangement of amino-acid residues must be taken into consideration in relating structure to biological function in the living cell even in comparatively small peptide molecules which do not appear to possess any ordered secondary or tertiary structure in aqueous solution.

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GROWTH PATTERNS IN *NEUROSPORA*

A Biological Clock in *Neurospora*

MANY fungi produce alternating zones of different growth type in response to diurnal light-cycles and temperature-cycles, and in some cases the zonation will continue to be produced for a time in continuous darkness and at a constant temperature. In 1953 Brandt[1] reported observation of zonation in the growth and conidia formation of *Neurospora crassa* mycelia in standard glass race-tubes maintained in constant darkness, humidity and temperature. Inspection of Brandt's photographs suggested to us that the zones were formed with a frequency of approximately one a day, and we have tested the implication that there does occur in *Neurospora* a typical biological daily clock—that is, a rhythmic system with an innate circadian ('about a day') period which is relatively independent of the temperature. (We are here adopting the suggestion (personal communication) of Prof. F. Halberg that the word 'circadian' obviates all the long-standing confusion inherent in the words diurnal, daily, 24-hr., as adjectives to describe the rhythms with which we are concerned.)

Brandt reported that he obtained zonation in only one (No. 21863, prolineless) strain of several that he examined; and that the zonation occurred on only one of the supplemented media ('Gray's') that would support growth of this strain. Zonation occurred at constant temperature either in a 24-hr. light–dark cycle, or in continuous darkness after a brief period of initial growth in white light. Zonation does not develop if the mycelium is maintained in continuous white light; but we have found that it can develop in continuous red (carbon) light.

In the experiments reported here the same strain and media as those used by Brandt were also used. Freshly inoculated race-tubes were placed in a temperature-controlled cabinet containing a 14-watt cool-white fluorescent lamp. About 40 hr. later, when the mycelium was growing well, the white light was discontinued and a red lamp was turned on. At this time and at 24 hr. intervals thereafter the advance of the mycelial front was observed (in the red light) and marked on the race-tube. When the growth had reached the end of the agar, the tube was removed from the growth cabinet and a densimeter device was used to measure relative density of the mycelium along its entire length. The observed phenomenon consists of alternating zones of sparse and dense mycelium. Preliminary experiments failed to reveal any significant difference in the linear growth increments in the 4-hr. intervals throughout any 24-hr. interval. The distribution of mycelial density has accordingly been converted from its observed spatial scale to a temporal scale. Regions of dense growth show up as minima on the densimeter graphs.

Fig. 1 illustrates the results so obtained from two typical race-tubes, one maintained at 31° C. and the other at 24° C. Table 1 summarizes more extensive data on the time-interval between successive minima on the densimeter graphs. This interval, which is the period of the rhythm, is about 22 hr. and is the same at the two temperatures.

The zonation of *N. crassa* thus is regulated by a rhythmic phenomenon which manifests the essential features of a biological clock[2]. The rhythm has an innate free-running period which is close to 24 hr. relatively independent of the temperature. The rhythm can be entrained by a 24-hr. light-cycle. In addition to possessing these functional prerequisites of a good chronometer, the rhythm also possesses other features of typical circadian systems: (1) The phase of the rhythm can be established by a single transition from light to dark; (2) as with many other plant rhythms, the manifestation of the rhythm is

Table 1. TABULATION OF TIME-INTERVALS BETWEEN ZONES (MEASURED AS TIME BETWEEN SUCCESSIVE MINIMA ON DENSIMETER GRAPHS) AT THE TWO TEMPERATURES STUDIED

No. of intervals at 24° C.	Length of interval (hr.)	No of intervals at 31° C.
	18	2
2	17	
2	20	2
	20·5	2
4	21	3
	21·5	4
11	22	6
	22·5	1
7	23	1
	23·5	1
2	24	2
	25	
1	26	
	26·5	1
22·03	Mean interval	21·66
1·48	Std. dev.	1·80

destroyed by continuous white light. We have not yet studied entrainment by temperature-cycles, or the transient[3] pattern following single light signals.

The *Neurospora* system appears potentially valuable for an attack on the basic problem of the nature of the oscillations that constitute the circadian clock. We do not interpret the presence or absence of zonation as a reflexion of the presence or absence of the clock, but rather as a coupling or uncoupling from the clock of the particular processes leading to zonation. Thus, it may be necessary to find some other manifestation of the basic rhythm which is present even when there is no zonation before one can make all the intriguing analyses that seem potentially possible. However, the possibility of genetic analysis, the feasibility of heterokaryon formation, and the fact that *Neurospora* can be grown on fully defined media are features which make the system uniquely useful. For example, the pattern of zonation in a heterokaryon between two strains with a previously established 12-hr. phase difference might resolve the question: Is the clock oscillation a nuclear or a cytoplasmic feature?

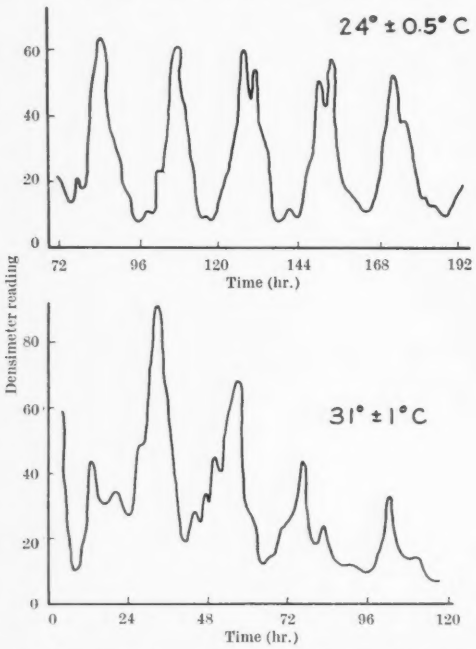

Fig. 1. Zonation in *Neurospora*. Zonation of the growth in a race-tube of a prolineless strain of *Neurospora* has been measured using a densimeter to record the relative density of mycelial growth. The time-scale shown represents hours elapsed after transfer of the race-tubes from white light to dim red light as described in the text

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C. S. PITTENDRIGH
V. G. BRUCE
N. S. ROSENSWEIG
M. L. RUBIN

Department of Biology,
Princeton University,
Princeton, New Jersey.

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Genetic Control of a Cyclic Growth Pattern in *Neurospora*

A STRAIN of *Neurospora* has been described which displays a daily cycle of growth morphology[1], and it has been demonstrated that this growth pattern reveals the presence in the organism of a temperature-independent biological clock[2]. The cyclic growth pattern consists of alternating regions of dense and sparse mycelium. Each dense region has a conspicuous tuft, or patch, of aerial growth on which orange macroconidia are produced. The pattern was demonstrated by strain 21863*a*, a proline-requiring mutant, when grown in race-tubes of Gray's medium[1]. Other strains grown in the same conditions produce a uniformly dense mycelium, and conidia formation occurs much later than in the tufts of 21863. This report concerns a study of the genetic control of this growth pattern. The cyclic growth condition will be termed 'patch', and the symbol will be *pat* ('tuft' has already been used for another phenotypic character).

Strain 21863*a* was crossed to wild-type 74*A*. Asci were dissected into ordered spore pairs. Eight complete asci (all four spore pairs growing) were classified for mating type, proline requirement, and patch (Table 1). The cyclic growth pattern segregated 2 : 2 in every ascus, as did mating type and proline requirement. Patch and proline requirement are controlled by separate genes which are not closely linked. On the other hand, patch showed close linkage to mating type; in these eight asci there was no recombination between them.

The mating type locus is in the left arm of linkage group I. Failure to metabolize nitrate is determined by a gene (*n-nit*) in the right arm[3]. The cross *pat a* × *n-nit A* was dissected, and thirteen complete asci were obtained. Their classification is shown in Table 2. The results indicate the patch locus is in the left arm of linkage group I, proximal to mating type.

Classification of the progeny of these crosses for patch was made in race-tubes of Gray's medium at 25° C.; the tubes were in constant light for 24 hr., then transferred to constant dark for 2–3 days before scoring. Tests in minimal medium[4] (supplemented

Table 1. 74 *A* (WILD-TYPE) × 21863*a* (*prol pat*)

No. of asci	Genotypes of ordered spore pairs
4	*prol*+ *pat*+ *A* *prol*+ *pat*+ *A* *prol* *pat* *a* *prol* *pat* *a*
2	*prol*+ *pat* *a* *prol*+ *pat* *a* *prol* *pat*+ *A* *prol* *pat*+ *A*
2	*prol*+ *pat*+ *A* *prol* *pat*+ *A* *prol*+ *pat* *a* *prol* *pat* *a*

Totals :

No. of spore pairs	Genotype	Growth on Gray's medium
10	*prol*+ *pat*+*A*	no lag
10	*prol* *pat* *a*	no lag
6	*prol*+ *pat* *a*	no lag
6	*prol* *pat*+ *A*	3 day lag

Note. Different patterns of second division segregation have been grouped together for brevity.

with proline) and in complete medium[5] were carried out in race-tubes in the same light and temperature conditions, but not all the *pat* segregants gave clear-cut cyclic growth patterns.

Normally, growth began quickly on Gray's medium and extended 1–4 cm. down the length of the race-tube after 24 hr. However, six of the cultures had a lag period of about three days before any growth appeared. These were the six proline-requiring *pat*+ segregants of the first cross (Table 1). There is thus a physiological interaction which might be described as partial suppression of *prol* by *pat* (though it could also be suppression by mating type gene *a*). Whether this interaction is related to the function of the biological clock is unknown. (The lag period occurred only on Gray's medium ; none of the cultures lagged on minimal medium plus proline or on complete medium.)

Table 2. *pat a* × *n-nit A*

No. of asci	Genotypes of ordered spore pairs	Simplest cross-over events required assuming following order of loci : I II III ...*A*, *a*...*pat*...centromere...*n-nit*..
4	*a pat* *n-nit*+ *a pat* *n-nit*+ *A pat*+ *n-nit* *A pat*+ *n-nit*	no crossing over
4	*a pat* *n-nit*+ *a pat* *n-nit* *A pat*+ *n-nit*+ *A pat*+ *n-nit*	single crossover in III
2	*a pat* *n-nit*+ *A pat*+ *n-nit*+ *a pat* *n-nit* *A pat*+ *n-nit*	single crossover in II
1	*a pat* *n-nit*+ *A pat* *n-nit*+ *a pat*+ *n-nit* *A pat*+ *n-nit*	single crossover in I
1	*a pat* *n-nit*+ *A pat*+ *n-nit* *a pat* *n-nit*+ *A pat*+ *n-nit*	2-strand double in II, III
1	*a pat* *n-nit*+ *A pat*+ *n-nit* *a pat* *n-nit* *A pat*+ *n-nit*+	3-strand double in II, III

Note. Different patterns of second division segregation have been grouped together for brevity.

The tests for proline requirement were made on plates containing the sugar sorbose ; this causes growth to remain restricted to the spot of the inoculum, rather than spreading over the plate. The use of sorbose medium allows as many as twenty-five growth tests to be performed on a single plate. It was observed that some of the test colonies did not remain confined on the sorbose plates, but were expanding radially 5–10 mm. per day. The 'sorbose-escape' condition turned out to be characteristic of the patch segregants. This was a consistent correlation ; all 42 *pat* progeny from the two crosses escaped on sorbose, while all 42 *pat*+ progeny remained confined on sorbose. There was no evidence of any cyclic pattern in the sorbose-escape colonies. Sorbose-escape was achieved even on plates held in constant light, a condition in which the cyclic growth pattern is not observed on Gray's medium.

The sorbose-escape classification demonstrates that the presence of the patch gene can be detected in a situation in which it is not visibly related to a biological clock. It is possible that the patch gene is not directly involved in the function of the biological clock, but, rather, effects a growth habit which reveals an underlying clock. However, this could only be determined conclusively by a demonstration of clock activity in a *pat*+ strain.

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D. R. STADLER

Department of Botany,
University of Washington,
Seattle 5, Washington.

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PROTHORACIC GLAND STIMULATION BY JUVENILE HORMONE EXTRACTS OF INSECTS

By DR. LAWRENCE I. GILBERT* and DR. HOWARD A. SCHNEIDERMAN
Department of Zoology, Cornell University, Ithaca, New York

THE juvenile hormone was first recognized as the agent which prevents maturation of young insects[1]. A second role for this hormone, discovered shortly thereafter, was in egg development where, in many insects, it is necessary for yolk deposition[2]. The present article describes what appears to be a third role for the juvenile hormone, namely, stimulation of the prothoracic glands. This tropic action has hitherto been assigned either to a hormone secreted by the insect's brain[3] or occasionally to low

* Present address : Department of Biological Sciences, Northwestern University, Evanston, Illinois.

temperature[4]. Experiments were conducted on pupæ of a variety of giant silk moths of the family Saturniidæ: *Hyalophora cecropia*, *Samia cynthia*, *Antherea polyphemus* and *Callosamia promethea*. Pupæ in two physiological states were employed as test objects: (*a*) diapausing pupæ which ordinarily remain for months in the pupal stage without developing; (*b*) pupæ which were stored at 5–8° C. for 5 months or more to activate their brains[3]. Such 'well-chilled' pupæ ordinarily initiate development within two weeks of being placed at 25° C. and emerge as adults 2½–3 weeks later.

In the first series of experiments, ether extracts were made of abdomens of male *H. cecropia* moths following Williams's procedure[5]. These ether extracts contain large amounts of juvenile hormone. When the extracts were injected into diapausing *S. cynthia* pupæ these moulted into second pupæ. For our present purposes the fact that the second moult was pupal is unimportant since a moult of a pupa in the presence of juvenile hormone will almost invariably be pupal. However, it is of interest that moulting occurred, for in our experience not one of thousands of diapausing *S. cynthia* pupæ has ever initiated adult development without prior chilling. Nevertheless, injection of 50 mgm. or more of ether extract invariably caused these diapausing pupæ to moult precociously into second pupæ or pupal-adult intermediates (Table 1*A*). Pupæ that received less than 50 mgm. failed to initiate adult development. Similar results were obtained with both newly moulted and older diapausing pupæ of *H. cecropia* and *A. polyphemus* (Table 1*B*). In all cases, the ether extracts terminated pupal diapause.

Table 1

Pupal weight (gm.)	Mgm. extract injected	Days to moult	Effect
(*A*) Moulting of unchilled seven-month-old diapausing *S. cynthia* pupæ after injections of ether extracts*.			
1·60	50	27	Adult-like intermediate
1·56	100	13	Second pupa
1·83	100	17	Second pupa
1·65	150	13	Second pupa
1·80	150	23	Pupa-like intermediate

* Uninjected controls did not initiate development after 6 months.

(*B*) Moulting of unchilled one-month-old diapausing pupæ of *H. cecropia* and newly moulted diapausing pupæ of *H. cecropia* and *A. polyphemus* after injections of ether extracts.

	H. cecropia (one month)*		
4·65	100	—	No development after 6 months
5·30	200	23	Adult-like intermediate
5·25	250	13	Pupa-like intermediate
5·45	400	17	Pupa-like intermediate
5·40	400	—	No development after 6 months
5·46	450	23	Pupa-like intermediate
4·80	600	23	Pupa-like intermediate
4·75	600	23	Pupa-like intermediate

* Uninjected controls did not initiate development after 6 months.

Hours after moulting	Mgm. extract injected	Days to moult	Effect
	H. cecropia (newly moulted)*		
4	100	—	No development after 6 months
12	300	19	Adult-like intermediate
36	100	31	Adult with few pupal characters
	A. polyphemus (newly moulted)*		
Prepupa	200	—	No development after 3 months
1	200	55	Adult-like intermediate
6	200	23	Adult-like intermediate
10	150	19	Pupa-like intermediate
12	250	33	Pupa-like intermediate

* Uninjected controls did not initiate development after 3 months.

In addition, when extracts were injected into 'well-chilled' pupæ they caused precocious moulting. Thus, results of more than 800 injections into well-chilled pupæ of *S. cynthia*, *C. promethea*, *H. cecropia* and *A. polyphemus* disclosed that pupæ receiving more than 50 mgm. of ether extract invariably moulted into second pupæ within 10–13 days. These several results suggest that the juvenile hormone or some other constituent of the ether extracts stimulates moulting.

To decide whether the ether extracts provoke moulting by stimulating the pupal brain or by directly stimulating the prothoracic glands, the following experiments were performed. A series of diapausing *H. cecropia* pupæ had their brains removed. This placed the pupæ in permanent diapause and such brainless pupæ never spontaneously initiate adult development. However, when three such brainless pupæ were injected with 200, 400 and 600 mgm. of ether extract, the two which received the largest injections moulted into second pupæ while the third remained in diapause (Table 2). Similar results were obtained with brainless *S. cynthia* pupæ (Table 2). From these experiments, it appears that large amounts of ether extract stimulate the prothoracic glands and so terminate pupal diapause.

Table 2

(*A*) Moulting of brainless diapausing pupæ of *H. cecropia* and *S. cynthia* after injections of ether extracts.

Pupal weight (gm.)	Mgm. extract injected	Days to moult	Effect
	H. cecropia		
6·73	200	—	Never initiated development
5·53	400	41	Second pupa
6·10	600	32	Second pupa
	S. cynthia		
1·90	100	13	Second pupa
3·21	250	15	Second pupa

An alternative explanation is that the ether extract contained some prothoracic gland hormone, ecdyson, and this reacted directly with the pupal tissues to initiate development. This possibility was tested by injecting a large series of isolated pupal abdomens of *S. cynthia* and *A. polyphemus* with 80–300 mgm. of ether extract. None of these preparations ever initiated development, although many survived as long as four months. Moreover, repeated efforts to extract ecdyson from the ether extracts have failed. These results seem to rule out the prothoracic gland hormone as the effective moult-promoting agent in the ether extracts. Hence, it seems safe to conclude that something in the ether extracts stimulates the insect's prothoracic glands.

To determine whether the factor which stimulated the prothoracic glands was the juvenile hormone itself, or some other substance, extracts in which juvenile hormone was concentrated 100–500-fold by various chemical procedures[6] were injected into chilled pupæ, diapausing pupæ and brainless pupæ. As Table 3*A* reveals, the concentrated juvenile hormone preparations had potent prothoracic gland-stimulating activity. Indeed, the prothoracic gland-stimulating factor was concentrated to about the same degree as the juvenile hormone by the chemical procedures we employed. Moreover, when brainless diapausing pupæ were injected with huge amounts of ether extract from which juvenile hormone had been removed by countercurrent distribution, they failed to respond (Table 3*B*). In short, procedures which concentrate the juvenile hormone, concentrate the

Table 3

(A) Precocious moulting of well-chilled *A. polyphemus* pupæ after injection of purified juvenile hormone extracts.

Pupal weight (gm.)	Mgm. extract injected	Days to moult	Effect
		Extract *A*	
4·19	2·3	13	Second pupa
5·26	5	12	Second pupa
5·15	8	10	Second pupa
4·90	15	13	Second pupa
		Extract *B*	
4·15	0·05	13	Second pupa
5·05	0·10	13	Second pupa
4·91	0·10	11	Second pupa

(B) Effect of juvenile hormone-free extracts on brainless diapausing *S. cynthia* pupæ.

3·20	180	—	Never initiated development
2·13	270	—	Never initiated development
2·19	300	—	Never initiated development
3·30	400	—	Never initiated development
2·80	450	—	Never initiated development

prothoracic gland-stimulating factor and procedures which remove juvenile hormone from extracts, also remove the prothoracic gland-stimulating factor. These results indicate that the juvenile hormone or a molecule with similar chemical properties, perhaps brain hormone, is the effective agent in the extracts that triggers off the prothoracic glands. Hence, we may conclude that either the juvenile hormone stimulates the prothoracic glands or the extract contains brain hormone in addition to juvenile hormone.

A final decision between these alternatives awaits tests with pure juvenile hormone preparations, but some insight is provided by two recent reports which were published when the present experiments were completed. Williams[7] has announced that implantation of active corpora allata terminates diapause in brainless diapausing *H. cecropia* pupæ. This important result is consistent with the view that the juvenile hormone itself is the effective agent in our extracts that activates the prothoracic glands. This prospect is made more attractive by the recent report of Kobayashi and Kerimura[8], which indicates that brain hormone extracted from the commercial silkworm has similar solubility properties to juvenile hormone. Thus it seems possible that brain hormone is similar chemically to juvenile hormone, and it is perhaps not too surprising that both hormones can activate the prothoracic glands. Whether or not the juvenile hormone actually functions in any immature insect to stimulate the prothoracic glands and cause moulting remains to be seen.

We wish to express our thanks to Dr. Berta Scharrer for her critical evaluation of this manuscript.

Note added in proof: Ichikawa, M., and Nishiitsutsuji-Uwo, J. (*Biol. Bull.*, **116**, 88; 1959), have shown that the corpora allata of *Philosamia cynthia ricini* can induce moulting in brainless pupæ. Their results indicate that, in addition to eliciting juvenile hormone, the corpora allata store neurosecretory material transported from the brain via the nervi corporis allati. They conclude that implants of larval and adult corpora allata furnish two hormones controlling post-embryonic development, namely, juvenile hormone and a moult-inducing hormone derived from the protocerebrum (brain hormone). These results suggest that extracts of male *H. cecropia* moths may contain brain hormone in addition to juvenile hormone.

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EVOKED POTENTIALS IN VISUAL CORTEX OF THE UNANÆSTHETIZED CAT

By GABRIEL HORN and JOHN BLUNDELL

Department of Anatomy, University of Cambridge, and Department of Neurology and Neurosurgery, McGill University and the Montreal Neurological Institute

RECENT work has indicated that when an animal 'attends' to a non-visual stimulus, photically evoked potentials in the visual pathway of the unanæsthetized cat are reduced[1]. It was concluded from these and other studies[2] that this depression of evoked responses implies a reduction of the sensory inflow which, if it occurs " . . . in all other sensory paths except the ones concerned with the object of attention, such an inhibitory mechanism might lead to the favouring of the attended object by the selective exclusion of incoming signals"[2]. It is not clear how, in the above experiments, 'attentive' behaviour was assessed, though in the studies of the visual system the cat's 'attention' was attracted, among other things, by a call or by fish odour delivered to the cage. When a cat is called, it may look toward the source of the voice: when a fish odour is blown into the cage the cat usually responds by sniffing and looking toward the source of the odour. If the animal failed to make these responses, it is not apparent how 'attentive' behaviour was otherwise assessed. Hence it is difficult to escape the conclusion that presentation of a non-visual stimulus may have resulted in the cat searching the visual field. The above experiments do not therefore exclude the possibility that the evoked responses were reduced in the modality actually being used for examining the sensory field.

The following experiments were undertaken to determine the changes in cortical evoked response to light flash in the unanæsthetized cat, when its behaviour was directed toward an object in the visual field (mouse) and to a non-visual stimulus (conditioned tone) respectively. Six cats were used. A monopolar electrode of approximately 1 mm. tip diameter was placed on the visual cortex using as indifferent electrode a screw driven into the frontal bone. Several days after operation the animal was put in a box illuminated by a 6-volt battery bulb.

Evoked responses to flash were displayed on an oscilloscope and filmed while the cat was resting facing the stroboscope. The flash, delivered once in approximately 2 sec., was of 1-m. sec. duration with an intensity of approximately 1 lambert. A mouse was introduced between stroboscope and cat, separated from the latter by a transparent plastic sheet. During the first few presentations of the mouse, the cat usually was intensely excited; but later it sat still, intently watching the mouse with little or no pilo-erection, or unsheathing of the claws. At this time 20 evoked responses to flash were recorded. Ten of these experimental responses were selected at random from the 20, together with 10 control evoked responses from the resting animal, recorded immediately before introduction of the mouse. The mean of each of these sets of results was calculated. These means for each animal were tabulated and the significance of any differences between experimental and control conditions obtained by applying a paired t test. It was found that when the cat was watching the mouse the electrocorticograph was flattened. The surface positive component of the primary wave of the evoked potential was decreased by 27 per cent ($P < 0.001$), and its duration reduced by 20 per cent ($P < 0.01$). The amplitude of the surface negative component was decreased by 21 per cent ($P < 0.02$). The excursion of the second wave of the response was reduced by 19 per cent ($P < 0.02$) and waves of the later components by 51 per cent ($P < 0.001$).

In order to orientate the cat's behaviour to a non-visual modality, the animal was conditioned to receive a slight shock to the fore-limbs after several tones, each delivered in the interval between consecutive flashes. The number of tones delivered prior to the shock was varied between 2 and 10 in any trial. After the first few trials, shocks were only occasionally applied. During the early stages of conditioning, at the onset of the tones, the cat looked intently around the box. At this time the electrocorticograph was reduced in amplitude. The surface positive component of the primary wave was reduced by 21 per cent ($P < 0.02$) and its duration by 19 per cent ($P < 0.02$): the amplitude of the second wave of the response was attenuated by 34 per cent ($P < 0.01$) and the later oscillations by 40 per cent ($P < 0.02$).

At a later stage of conditioning, the cat did not look around the box during the tones, but remained still except for some slight shifting of the fore-limbs, twitching of the facial muscles and flicking of the ears. Occasionally at this stage the cat got up during the tones and settled in another part of the cage. Measurement of records taken when the animal showed minimal movement and when its response to the acoustic stimulus was accompanied by little or no visual searching component showed that the amplitude of the electrocorticograph was diminished. The amplitude and duration of the evoked responses were not, however, significantly different from those recorded under control conditions.

From the above results it appears that photically evoked responses in the visual cortex are not attenuated when a cat's behaviour is orientated to an acoustic stimulus, so long as there is no visual searching component in the animal's behavioural response. On the other hand, when the animal's behaviour is directed to a stimulus in the visual field, or shows some visual searching component in its response to a non-visual stimulus, evoked potentials are reduced in amplitude. It might be argued that when the cat was looking at a mouse the information contained in the flash was irrelevant and so attenuated. However, when the animal's behaviour was directed to the acoustic stimulus, in the absence of visual searching activity, the information from the flash was likewise irrelevant. The evoked potentials in these two situations should therefore have been treated similarly. They were not.

Reduction in amplitude of an evoked response to a given photic input may be brought about in one or more ways (for example, inhibition, reduction of facilitation, occlusion). Whatever the mechanism, one of the effects of such activity may be, in some circumstances, to increase sensory contrast and so improve the sharpness of input boundaries. Absence of such input attenuating activity in the visual system, as when behaviour is directed to an acoustic stimulus, could give a greater absolute sensitivity in the visual pathway. The animal would thus monitor its environment more sensitively so providing central mechanisms with a maximum of information on which to act.

One of us (G. H.) wishes to thank the Wellcome Trust and the National Research Council of Canada for grants toward the cost of travel expenses. Thanks are also due to Prof. H. Jasper for his interest in this work.

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INFLUENCE OF UNBALANCED GROWTH ON SUBSEQUENT X-RAY-INDUCED INHIBITION OF DEOXYRIBONUCLEIC ACID SYNTHESIS IN *ESCHERICHIA COLI* 15_T-

By DANIEL BILLEN

Department of Biology, Section of Microbiology, University of Texas, M. D. Anderson Hospital and Tumor Institute, Houston, Texas

In an earlier report[1] it was demonstrated that the number of survivors among X-irradiated *Escherichia coli* strains *B/r* and 15_T- (thymine-less) was increased when log-phase cells were incubated in the presence of chloramphenicol prior to X-ray exposure. In the case of *E. coli* 15_T- deoxyribonucleic acid synthesis was necessary for the development of radioresistant cells, since when deoxyribonucleic acid synthesis was prevented by the removal of thymine from the pre-irradiation incubation medium, radioresistance was not enhanced by chloramphenicol. One interpretation of these results was that 'surplus' deoxyribonucleic acid formed in the presence of chloramphenicol (higher ratio of deoxyribonucleic acid/protein than in non-treated cells) was biologically active and increased the number of sensitive sites

in the bacterium[1]. An additional possibility considered was that pretreated cells, unbalanced in macromolecular constituents, were in special physiological states such that the probability of overcoming X-ray induced lesions was increased. Using cells in the several unbalanced states with regard to protein, deoxyribonucleic acid, and ribonucleic acid levels we have studied deoxyribonucleic acid synthesis after X-ray exposure of such cells. In the present work results are presented which show: (1) An inhibition by chloramphenicol of phasing or 'synchronization' of the deoxyribonucleic acid-synthesizing system and (2) that the radiosensitivity of the synthesizing mechanism is altered by previous chloramphenicol exposure.

The conditions for obtaining log phase as well as establishing 'unbalanced phase' growth were those previously described[1]. Following the various treatments to be described for obtaining unbalanced growth, the cells were cooled in an ice-bath, harvested, washed and resuspended in cold minimal-salts–glucose medium to give a final concentration of about 20 times the original number ($1–2 \times 10^{10}$ cells/ml.) in order to obtain satisfactory levels of material for chemical analysis. The concentration of cells during exposure was higher than the level used in the earlier studies by a factor of approximately 100; as a result the number of colony-formers found after a dose of 10,000 r. was higher in the experiments reported here[2,3]. Following X-ray exposure at ice-bath temperature the cells were added to twice the original culture volume of pre-warmed minimal medium supplemented with 20 μgm./ml. thymine and re-incubated with aeration at 37° C. Aliquots of this culture were removed at intervals for analysis as detailed earlier[1].

Prior to treatment with 10,000 r. of X-rays, log phase *E. coli* 15T⁻ cells were incubated in minimal medium at 37° C. for 1 hr. under the following conditions: (*A*) incubation in the presence of thymine (normal log-phase cells); (*B*) incubation in the presence of 10 μgm./ml. chloramphenicol and (1) plus thymine (increased ribonucleic and deoxyribonucleic acid/protein content), or (2) without thymine (increased ribonucleic acid/deoxyribonucleic acid and protein content); (*C*) incubation in the absence of thymine (increased ribonucleic acid and protein/deoxyribonucleic acid content).

In normal log-phase *E. coli* 15T⁻ (condition *A*) exposed to 10,000 r. of X-rays, deoxyribonucleic acid synthesis proceeded rapidly for 30–60 min. (Fig. 1). This was followed by a period in which no net synthesis was detectable. In other experiments in which survival was higher than that found in the experiment from which the data of Fig. 1 were taken, renewed synthesis was sometimes seen by 90 min. The number of colony-forming cells in the irradiated suspensions (10–25 per cent of the controls) remained constant or showed a slight decline during the first 30 min. A rapid increase then occurred that probably accounted for the renewed synthesis observed in some experiments.

When chloramphenicol was added to log-phase cells (condition *B*1) ribonucleic and deoxyribonucleic acids continued to accumulate while protein synthesis was largely inhibited[1]. Such cells washed free of the antibiotic and re-incubated in a thymine-supplemented minimal medium showed a delay of approximately 30 min. before net deoxyribonucleic acid synthesis was resumed (Fig. 1). When the washed cells treated with chloramphenicol were exposed to 10,000 r. of

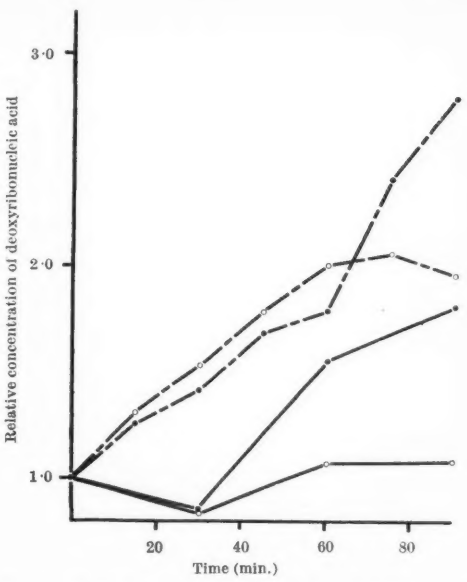

Fig. 1. The influence of prior chloramphenicol treatment on subsequent deoxyribonucleic acid synthesis. Prior to treatment with 10,000 r. of X-rays, log-phase *E. coli* 15T⁻ cells were incubated for 1 hr. under the following conditions: ●- - -●, normal log-phase cells (condition *A* of text); ○- - -○, condition *A*, and then exposure to 10,000 r.; ●——●, exposed to chloramphenicol (condition *B*1); ○——○, condition *B*1, then exposure to 10,000 r.

X-rays and then resuspended in thymine-supplemented medium no net increase in deoxyribonucleic acid content was observed during the 2 hr. the cultures were studied (only the first 90 min. are shown in Fig. 1). A similar result was found for cells washed free of thymine prior to incubation in thymine-free minimal medium to which chloramphenicol has been added (condition *B*2). During such incubation only ribonucleic acid was observed to accumulate in large amounts during the 1 hr. exposure to the antibiotic[1]. As seen in Fig. 2, deoxyribonucleic acid synthesis in such cells was completely suppressed after X-ray exposure.

Log-phase cells, washed free of thymine and then re-incubated for 1 hr. at 37° C. in thymine-free minimal medium (condition *C*), showed a marked increase in ribonucleic acid and protein nitrogen while deoxyribonucleic acid synthesis was essentially nil[1]. This was the 'unbalanced growth' reported for this strain of *E. coli* by Barner and Cohen[4]. Following this treatment the cells, after harvesting and washing at ice-bath temperatures, appeared to be synchronized[5] with respect to deoxyribonucleic acid synthesis (Fig. 2). The deoxyribonucleic acid nearly doubled in 30 min. This was followed by a period of reduced deoxyribonucleic acid synthesis before a new rate of deoxyribonucleic acid accumulation was seen. X-irradiation did not greatly alter the synthesis during the initial doubling period (Fig. 2). However, after this initial burst no further increment was found during 120 min. of observation. The loss of acid-insoluble deoxyribonucleic acid observed in the irradiated cell culture after 60 min. was due to lysis of a portion of the cells as reflected by a decreased turbidity of the cultures as well as a reduction in the harvested cell yield (protein). The surviving cells did not grow at a sufficiently

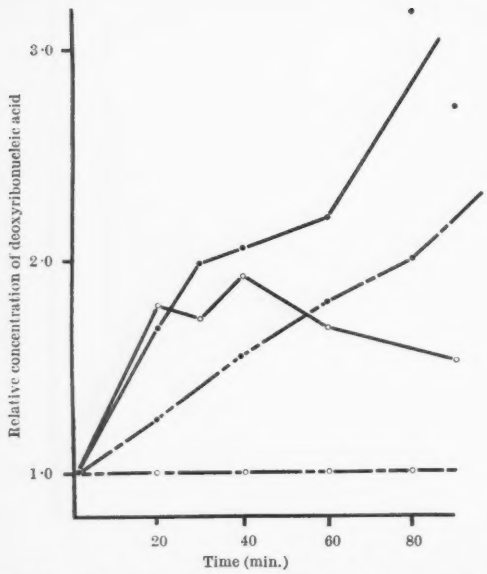

Fig. 2. The effect of thymine starvation during chloramphenicol exposure on subsequent deoxyribonucleic acid synthesis. Prior to treatment with 10,000 r. of X-rays, log-phase *E. coli* 15*T*- cells were incubated for 1 hr. under the following conditions: ●——●, incubation in the absence of thymine (condition *C* of text); ○——○, condition *C*, and then exposure to 10,000 r.; ●---●, exposed to chloramphenicol in the absence of thymine (condition *B*2); ○---○, condition *B*2, and then exposure to 10,000 r.

rapid rate to be reflected in the analysis during these 2 hr. It required more than 2 hr. for dividing survivors to reach the initial level of unirradiated cells of the controls.

Thus, during the incubation in the absence of thymine (condition *C*), a radioresistant synchronization of deoxyribonucleic acid appeared to have occurred. Similar treatment did not synchronize ribonucleic acid or protein synthesis[6]. The addition of chloramphenicol to such cells prevented the development of the radioresistant system synthesizing deoxyribonucleic acid. It is also apparent that the addition of chloramphenicol to log-phase *E. coli* 15*T*- incubated in the presence of thymine resulted in a physiological state such that deoxyribonucleic acid synthesis did not occur immediately after removal of the antibiotic. Cells in this physiological state could not synthesize deoxyribonucleic acid until a radiosensitive process had been initiated. Although the mechanism whereby chloramphenicol brings about this effect is unknown, it is tempting to speculate that the antibiotic-induced inhibition of protein synthesis was involved. The protein (and/or ribonucleic acid) synthesized in a given time period (in the presence or absence of net deoxyribonucleic synthesis) may be a necessary prerequisite for subsequent deoxyribonucleic acid synthesis. One may envisage this protein as being involved in the formation of a template[7–10] or as specific enzymes perhaps similar to the polymerases described by Kornberg and collaborators[11] which were found to be capable of *in vitro* deoxyribonucleic acid synthesis. Additional experiments planned may provide further insight into the true nature of the radiosensitive process inhibited by chloramphenicol.

The results with irradiated *E. coli* 15*T*- correlate well with the findings of others in plant[12] and animal[13,14] studies that there is a radiosensitive process involved in deoxyribonucleic acid synthesis which is not the deoxyribonucleic acid replication system itself. The radiosensitive process occurring prior to actual deoxyribonucleic acid synthesis may involve protein synthesis as suggested from the results presented here. Log- or stationary-phase cell suspensions when exposed to X-rays contain organisms in various phases of their division cycle. One may speculate that there occurs, in normal growth of individual cells, a phase such that the products of the radiosensitive process are exhausted and must be synthesized anew before deoxyribonucleic acid replication can proceed. If most cells of an exposed population were in the active deoxyribonucleic acid synthesizing (radioresistant) phase they would continue to make deoxyribonucleic acid until a predetermined level would have been reached. Therefore at doses of X-rays in which most of the population no longer were colony-forming cells a good amount of deoxyribonucleic acid as well as ribonucleic acid and protein synthesis would occur[6]. The extent of deoxyribonucleic synthesis would be determined by the length of the deoxyribonucleic synthetic period relative to that of the sensitive pre-synthetic phase. In a log-phase population most cells would be in the deoxyribonucleic acid synthesizing phase if this period occupied most of the division cycle of the cell. Based on this model our results would suggest that most log-phase cells are not in the radiosensitive period since irradiated populations increased significantly their deoxyribonucleic acid-levels upon reincubation. The radiosensitive pre-synthetic process, having been inhibited by radiation exposure, would no longer function and thus deoxyribonucleic acid synthesis would come to a close if it is assumed that the radiosensitive process is permanently inhibited by irradiation. When sufficient numbers of survivors were present these would grow at a rate reflecting their physiological state prior to exposure and eventually produce measurable amounts of deoxyribonucleic acid. If the number of survivors were high enough and exhibited little lag upon resuspension in a complete growth medium they would produce sufficient amounts of deoxyribonucleic acid to be measurable soon after exhaustion of deoxyribonucleic acid synthesis in dying cells. Thus the termination of deoxyribonucleic acid synthesis in dying or dead cells would be masked by the dividing viable cells. At higher doses of X-irradiation deoxyribonucleic acid synthesis may be completely suppressed by the destruction of the radioresistant deoxyribonucleic acid synthesizing mechanism itself[6].

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APPOINTMENTS VACANT

APPLICATIONS are invited for the following appointments on or before the dates mentioned :

ASSISTANT LECTURER IN CHEMISTRY at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (September 30).

ASSISTANT LECTURER (with an honours degree in geology and with ability to lecture in historical geology and micro-palæontology) in GEOLOGY at the University of Canterbury, Christchurch, New Zealand—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (September 30).

ASSISTANT LECTURER IN SOCIAL ADMINISTRATION—The Registrar, The University, Manchester 13 (September 30).

ASSISTANT LECTURERS IN BOTANY—The Registrar, The University, Manchester 13 (September 30).

CHAIR OF EDUCATION in the University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (September 30).

SENIOR LECTURER IN THE DEPARTMENT OF GEOPHYSICS at the University of the Witwatersrand, Johannesburg, South Africa—The Secretary, Association of Universities of the British Commonwealth, 36 Gordon Square, London, W.C.1 (September 30).

SENIOR LECTURER or LECTURER (with an honours degree in engineering and preferably with some professional experience since graduation) IN MECHANICAL ENGINEERING—The Registrar, King's College, Newcastle upon Tyne (September 30).

READER or SENIOR LECTURER (wtih experience in experimental physics, experience in some aspects of applied physics would be of particular value) IN THE DEPARTMENT OF PHYSICS, to help arrange, and to take part in, the teaching of physics to engineers at all levels—The Registrar, The University, Manchester 13 (October 5).

DIRECTOR (with a wide scientific background) OF THE COMPUTATION CENTRE—The Vice-Principal, McGill University, Montreal, Que., Canada.

LECTURER (with a good honours degree and some practical experience, preferably in the field of structural steelwork ; some teaching experience would be an advantage) IN THE DEPARTMENT OF CIVIL ENGINEERING—The Registrar, The University, Bristol.

LECTURER (with an honours degree in chemistry and postgraduate experience of academic or industrial research) IN INORGANIC CHEMISTRY—The Secretary, Sir John Cass College, Jewry Street, London, E.C.3.

REPORTS and other PUBLICATIONS

(not included in the monthly Books Supplement)

Great Britain and Ireland

Sir John Cass College. Report, Session 1957–58. Pp. 22. (London : Sir John Cass College, 1959.) [55

Government of Northern Ireland : Ministry of Agriculture. Leaflet No. 91 : Parasitic Worm Diseases of Farm Livestock. Pp. 6. (Belfast : Ministry of Agriculture, 1959.) [55

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LETTERS TO THE EDITORS

GEOPHYSICS

Great Earthquakes and the Astronomical Positions of Uranus

THANKS to the excellent collection of uniform data of earthquakes given by Gutenberg and Richter[1], it is now easily possible to study statistically the influence of different factors on earthquakes. In the course of a study of tidal effects on earthquakes[2], the astronomical positions of the planets have also been taken into account and a remarkable correlation between the positions of Uranus and the moment of great earthquakes has been established for a certain period. Gutenberg and Richter's data of all earthquakes equal or greater than magnitude $7\frac{3}{4}$ have been used. The investigations will be published in detail later, but here attention is directed to the results concerning the position of Uranus.

A total of 134 earthquakes has been investigated. In this a fairly significant amount of cases has been found, where Uranus was very near its upper or lower transit of the meridian of the epicentre in the time of great earthquakes. Closer investigation showed that this occurred especially during the years 1904, where Gutenberg–Richter's data start, and also 1905 and 1906. The results for this period are given in Table 1, which contains the data for the earthquakes and also the Right Ascension of the meridian of the epicentre at the time of the earthquake and the position and the meridional distance in Right Ascension of Uranus at that time. The latter data have been divided into two groups. Group I contains all the cases when Uranus is within a distance of $\pm$ 1h. from upper or lower transit through the meridian; group II comprises all cases with greater meridional distances, that is, within $\pm$ 1h. to $\pm$ 6h. The probability of Uranus being found in group I is one-sixth of the total cases and that for group II is five-sixths of the total, if the distribution of the times of the earthquakes is entirely by chance. As Uranus completes each day very approximately all the possible meridian distances, there occurs within the period of 1,090 days, represented in Table 1, a total of 2,180 transits (upper and lower). Therefore, if the times of occurrence of earthquakes are distributed by chance, a uniform distribution of the positions of Uranus can be expected. This is corroborated by the fact that the positions of the Sun or the Moon show no significant deviation from pure chance; for example, in Table 1 the Sun is found to be five times near transit, which is very near the expected value for chance distribution of group 1. But the result for Uranus is quite different and unexpected.

Table 1. GREAT EARTHQUAKES: $M \geqslant 7\frac{3}{4}$

No.	Date	G.M.T.	Lat.	Long.	Local time	R.A. Mer.	R.A. Ur.	Uranus mer. dist. (I)	Uranus mer. dist. (II)	Remarks
		h. m. s.			h. m.	h. m.	h. m.	h. m. h.	h. m. h.	
	1903									
1	Dec. 28	2 56 00	7° N.	127° E.	11 24	17 46	17 44	−0 02		Epicentre ± 5°. Sun near transit
	1904									
2	Jan. 20	14 52 06	7 N.	79 W.	9 36	17 30	17 50	+0 20		
3	June 25	14 45 36	52 N.	159 E.	1 22	19 35	17 50		−1 45	
4	June 25	21 00 30	52 N.	159 E.	7 36	1 51	17 50		+4 00+12	
5	June 27	00 09 00	52 N.	159 E.	10 45	5 04	17 49	+0 45+12		
6	Aug. 24	20 59 54	30 N.	130 E.	5 40	3 51	17 43		+1 52+12	
7	Aug. 27	21 56 06	64 N.	151 W.	11 52	10 15	17 42		−4 32+12	Sun in transit
8	Dec. 20	05 44 18	8·5 N.	83 W.	0 12	6 06	18 00	−0 06+12		Sun in transit
	1905									
9	Jan. 22	02 43 54	1 N.	123 E.	10 56	18 59	18 08	−0 51		
10	Feb. 14	08 46 36	53 N.	178 W.	20 55	6 29	18 13	−0 16+12		
11	April 4	00 50 00	33 N.	76 E.	5 54	18 41	18 18	−0 23		Kangra
12	June 2	05 39 42	34 N.	132 E.	14 28	7 08	18 13	−0 55+12		
13	July 6	16 21 00	39·5 N.	142·5 E.	1 51	20 47	18 08		−2 39	
14	July 9	09 40 24	49 N.	99 E.	16 16	11 23	18 07		−5 16+12	
15	July 23	02 46 12	49 N.	98 E.	9 18	5 19	18 05	+0 46+12		
	1906									
16	Jan. 21	13 49 35	34 N.	138 E.	23 02	7 02	18 26	−0 36+12		
17	Jan. 31	15 36 00	1 N.	81·5 W.	10 10	18 50	18 28	−0 22		Greatest earthquake
18	April 18	13 12 00	38 N.	123 W.	5 00	18 43	18 37	−0 06		San Francisco
19	Aug. 17	00 10 42	51 N.	179 E.	12 07	9 45	18 21		−3 24+12	Sun in transit
20	Aug. 17	00 40 00	33 S.	72 W.	19 52	17 30	18 21	+0 51		
21	Sept. 14	16 04 18	7 S.	149 E.	2 00	1 31	18 20		+4 48+12	
22	Nov. 19	07 18 18	22 S.	109 E.	14 34	18 24	18 27	+0 03		
23	Dec. 22	18 21 00	43·5 N.	85 E.	0 01	6 03	18 35	+0 33+12		Sun in transit

+ zh., Uranus culminates zh. later; + 12h., lower transit; R.A.Mer., Right Ascension of meridian at the time of earthquake; Local time, local sideral time at the time of earthquake.

Table 2

No.	Date	G.M.T.	Lat. ° N.	Long. ° E.	Local time	R.A. Mer.	R.A. Ur.	Uranus merid. dist.	Place	Magnitude
		h. m. s.			h. m.	h. m.	h. m.	h. m. h.		
	1923									
1	Sept. 1	02 58 36	35·25	139·5	12 17	10 54	23 09	+0 16+12	Tokio	8·2
	1933									
2	Mar. 2	17 30 54	39·25	144·5	03 09	13 49	01 19	−0 30+12	Honshu	8·5
	1950									
3	Aug. 15	14 09 30	28·5	96·5	20 35	18 09	06 35	+0 25+12	Assam	8·6

Of 23 cases, listed in Table 1, not less than 15 belong to group I and only 8 are in group II. The expected number for group I would be 3·8. Application of the chi-square test gives $\chi^2 = 41$; with Yates's correction $\chi^2 = 37$, that is, for one degree of freedom, a probability much less than 0·0001 for its being a chance distribution. The deviation is therefore highly significant. The fact should be stressed that Table 1 is complete, that is, it includes all the earthquakes of magnitude equal to or greater than $7\frac{3}{4}$ (including intermediate and deep shocks) which occurred during this period.

Two points must be cleared up. First, for how long does the period extend with this marked correlation, and secondly, how far is it characteristic of Uranus? Or does the period include some other cosmic direction which only accidentally coincides with the position of Uranus during this period of observation? Regarding the first point, it can be stated that after 1906 the correlation becomes less significant, but it remains greater than average. As an example, Table 2 shows the meridional distance of Uranus for three remarkable earthquakes of later years, when the position of Uranus had already greatly changed. No. 1 is the Tokyo earthquake in the course of which 100,000 people were killed and 500,000 houses were destroyed. No. 2 is the second largest earthquake of the first half of this century (the greatest is No. 17 in Table 1) and No. 3 is the famous Assam earthquake (*Nature*, 167, 128; 1951). In each of these cases Uranus is near the meridian—not farther away than 30 min. from its lower transit. There is a certain difficulty in extending the investigation back to the years before 1904, as in many cases the epicentres are either not known or only very inaccurately. A collection of data has been given by Gutenberg[3]. Using his data and limiting the investigations to all cases where the epicentres are known with an accuracy of at least $\pm 5°$ of their geographical position, their number is 23 for the years 1900–3. In eight cases the position of Uranus is in group I; the expected number is 3·8. Therefore, the correlation extends back to 1900, but with diminished significance.

It should be mentioned that the years 1904–6 corresponded to a conspicuous maximum of energy release by the Earth through earthquakes. According to Gutenberg[3], the annual release during each of these years is 10·6; 22·2 and 34·1, against 6 in 1903 and 4·9 in 1907 (in units of 10^{24} ergs).

So far as the role of Uranus is concerned, it may be noted that the planet was nearly symmetrically opposed, during these years, by Neptune and Pluto and went into direct opposition to Neptune in 1906. The cases of 1906 are therefore also cases where Neptune was simultaneously near its transit at the times of the earthquakes. An opposition of Sun, Venus and Mars to Uranus also occurred at the time of the Tokyo earthquake (Table 2).

The correlation cannot be explained by a tidal effect, since the statistical investigation for all the great earthquakes ($M = 7\frac{3}{4}$) during 1904–50 in regard to the absolute and relative positions of the Sun and the Moon give no indication of a significant deviation from chance distribution. The tidal forces of the planets are extremely small compared with those of the Sun and the Moon. That the accumulated stresses within the Earth's crust are released at times which, at least for a period of several years, are strongly correlated with certain positions of Uranus may, therefore, not be a relationship of cause and effect in the usual mechanical sense.

R. Tomaschek

Breitbrunn/Chiemsee,
Bavaria.
March 27.

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Air Density in the Upper Atmosphere from Satellite Orbit Observations

From the rate of change of period of a satellite, it is possible to derive the density of the atmosphere at the altitude of the perigee of the orbit. Now that some ten successful satellite launchings have taken place, giving orbits with various perigee heights, the variation of air density with height can be derived over a considerable range of altitude. Many perigee heights have been less than 230 km., the exceptions being *Explorer* IV (1958 ζ) at 260 km; *Explorer* I (1958 α) at 365 km., *Vanguard* I (1958 β 2) at 656 km., and the recently launched *Vanguard* II (1959 α) at 558 km. The air density at greater heights is therefore less well established. From an analysis of data from six different satellites, the smoothed set of values in Table 1 has been derived. The accuracy, estimated by fitting a quadratic variation with height to the logarithm of the density, is of the order of 20 per cent at the lower heights and 50 per cent at the greater heights.

Table 1. Values of Air Density derived from Observations on Satellites 1957 α_2, β and 1958 α, β_2, γ and δ

Height (km.)	Air density (gm./c.c.)	Height (km.)	Air density (gm./c.c.)
150	$1·2 \times 10^{-13}$	450	$3·8 \times 10^{-15}$
200	$3·8 \times 10^{-13}$	500	$1·9 \times 10^{-15}$
250	$1·4 \times 10^{-13}$	550	$9·6 \times 10^{-16}$
300	$5·0 \times 10^{-14}$	600	$5·3 \times 10^{-16}$
350	$2·0 \times 10^{-14}$	650	$3·2 \times 10^{-16}$
400	$8·4 \times 10^{-15}$	700	$2·0 \times 10^{-16}$

Above 300 km., the values of air density depend chiefly on the *Explorer* I and *Vanguard* I observations. After this analysis had been carried out, the rate of decrease of period for these two satellites increased comparatively rapidly to a new nearly constant value. The increase amounted to a factor of 1·51 for *Explorer* I and to a factor of 2·52 for *Vanguard* I, showing the effect to increase with height. For *Vanguard* I. the slope of the period – time curve has recently returned to its original value; and the local time at perigee, while the slope had the greater value, ranged from about 12.00 hr. to 18.30 hr. For *Explorer* I, the slope has also returned to its original value and is at present about to change again, the greater value being maintained for approximately the same range of local time as *Vanguard* I. If this change is attributed to a variation in air density, then the values in Table 1 need to be increased by the above factors when local time lies in the range 12.00–18.30 hr.

The scale height of the atmosphere H is the height interval over which the density changes by an exponential factor. Values for H in the region of 200 km. have been deduced in the following three ways.

(1) From the above density – height profile. H is obtained[1] as 46 ($\pm$ 5) at 200 km. H increases with

height and values of 52, 61, 72 and 89 km. are obtained for 300, 400, 500 and 600 km. altitude, but the observations are too scanty to enable the accuracy of these values to be estimated. The gradient of the scale height at 200 km. is obtained as 0·06 km./km.

(2) From the decrease in perigee distance. From *Explorer* III, H is obtained[2] as 39 ($\pm$ 9) km. at 180 km., and from *Atlas* (1958 ζ) as 36 km. to within a few kilometres for the same altitude.

(3) From the change in perigee height due to the Earth's equatorial bulge[3]. This method is suitable for satellites at approximately the inclination of the Russian artificial satellites, when the perigee moves slowly around the orbit and a significant part of the change in perigee height arises from the Earth's equatorial bulge. From *Sputnik* II, H is obtained[2] as 36 ($\pm$ 15) km. For *Sputnik* III rocket (1958 δ_1), methods 2 and 3 lead to inconsistent values.

A few rocket measurements of air density at the 200-km. level exist for comparison with the satellite values. A value of $2{\cdot}7 \times 10^{-13}$ gm./c.c. at 200 km. has been reported[4] from a U.S.S.R. rocket firing at 50° N. The Viking 7 flight in August 1951 at White Sands, New Mexico, gave[5] $1{\cdot}4 \times 10^{-13}$ gm./c.c. (to within a factor of 2) for the density and 43 km. for the scale height at 200 km. The latitude of White Sands is 36° N., and most of the observations upon which Table 1 is based refer to perigee latitudes between 36° N. and 33° S. The agreement between the scale heights is very close and that between the densities is just acceptable. On the other hand, an *Aerobee-Hi* fired in July 1957 at Fort Churchill, latitude 59° N., gave[6] $7{\cdot}0 \times 10^{-13}$ gm./c.c. ($\pm$ 30 per cent) for density and 94 km. for scale height at 200 km. altitude. A considerable latitude effect is therefore indicated at higher latitudes, and there is clearly a need for satellites with orbital inclinations near 90°, so that densities may be determined at the highest latitudes. Two further Fort Churchill firings have given[7] a winter-day value of $3{\cdot}6^{+3}_{-1{\cdot}5} \times 10^{-13}$ gm./c.c. and a winter night value of $1{\cdot}3 \pm 0{\cdot}6 \times 10^{-13}$ gm./c.c. at 202 km.

At the 200-km. altitude, the scale height seems to be in the region of 40 km. for equatorial and subtemperate latitudes. The corresponding temperature for an assumed molecular weight of air of 25 would be 1,100° K.

The results given here agree closely with those of D. G. King-Hele[8].

Acknowledgement is made to the Smithsonian Institution, the Naval Research Laboratory, Washington, and the Royal Aircraft Establishment, Farnborough, for their issues of orbital data on which these calculations have been based.

G. V. Groves

Department of Physics,
University College,
London, W.C.1.
June 17.

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PHYSICAL SCIENCES

A Special Case of the Superposition of Crystal Plates between Crossed Polars and its Bearing on the Microscopy of Cellulosic Fibres

When monochromatic light is passed at perpendicular incidence through two superposed and differently orientated transparent crystal plates between crossed polars, the intensity of the light transmitted by the analyser relative to that of the light entering the plates is given by the following expression, as was shown by Fresnel:

$$\begin{aligned} I = & -\sin2(\psi_2 - \psi_1)\sin2\psi_1\cos2\psi_2\sin^2(\delta_1/2) \\ & +\sin2(\psi_2 - \psi_1)\cos2\psi_1\sin2\psi_2\sin^2(\delta_2/2) \\ & +\cos^2(\psi_2 - \psi_1)\sin2\psi_1\sin2\psi_2\sin^2(\delta_1/2 + \delta_2/2) \\ & -\sin^2(\psi_2 - \psi_1)\sin2\psi_1\sin2\psi_2\sin^2(\delta_1/2 - \delta_2/2) \end{aligned} \quad (1)$$

where I is the relative intensity as just defined, ψ_1, ψ_2 are, respectively, the angles made by the corresponding vibration directions of the plates (that is, either the 'slow' or the 'fast' directions) with the vibration direction of the polarizer, and δ_1, δ_2 are the phase differences produced by the plates. (The expression ignores any reduction in the intensity due to absorption by the analyser, such as occurs in polaroid, but for a given analyser this reduction is by a constant factor, and does not affect the arguments which follow.) If the plates are of equal thickness and birefringence, $\delta_1 = \delta_2 = \delta$, and the fourth term in the expression vanishes. If also we put 2θ for the angle between the corresponding vibration directions, say the 'slow' directions, of the plates, and α for the angle between the bisectrix of 2θ and the vibration direction of the polariser (Fig. 1), the expression can be reduced to the form:

$$\begin{aligned} I = & \ 4\cos^4(2\theta)\sin^2(\delta/2)\cos^2(\delta/2)\sin^2(2\alpha) \\ & -4\sin^2(2\theta)\cos^2(2\theta)\sin^2(\delta/2)\cos^2(\delta/2)\cos^2(2\alpha) \\ & +4\sin^2(2\theta)\cos^2(2\theta)\sin^2(\delta/2) \end{aligned} \quad (2)$$

(This involves making use of the following equalities: $(\psi_2 - \psi_1) = 2\theta$; $\psi_1 = (\alpha - \theta)$; $\psi_2 = (\alpha + \theta)$; $\sin 2(\alpha - \theta)\cos2(\alpha + \theta) - \cos2(\alpha - \theta)\sin2(\alpha + \theta) = -\sin(4\theta)$; $\sin^2\delta = \sin^22(\delta/2) = 4\sin^2(\delta/2)\cos^2(\delta/2)$.)

By differentiating I with respect to 2α, and equating to zero, it can be shown that in the general case I has a minimum value when $\alpha = 0°, 90°, \ldots$ etc., and a maximum value when $\alpha = 45°, 135°, \ldots$ etc., that is that the pair of plates 'extinguishes' when the bisectrix OB (Fig. 1) is parallel or perpendicular to the polarizer vibration direction OP, and shows maximum brightness when in the 45° positions.

Three special cases arise. Two of these are familiar; in one $2\theta = 90°$, so that the two plates exactly compensate one another, and in the other $\delta = 0°$, or $n \times 360°$, where n is a whole number. In both these cases $I = 0$ for all values of α. The third case is that in which $\delta = 180°$, or $(n \times 360°) + 180°$, and the purpose of this note is to draw attention to it, since its consequences do not appear to be generally realized. In this case the first two terms of equation (2) vanish, since they both contain $\cos^2(\delta/2)$ which is now zero. The intensity is given by the third term alone, which does not contain α, and which simplifies to:

$$I = 4\sin^2(2\theta)\cos^2(2\theta) = \sin^2(4\theta) \quad (3)$$

since $\sin^2(\delta/2) = 1$. The intensity of the component which passes the analyser therefore remains constant as α varies, that is as the plates are rotated in unison

in their own plane between the polars, as for example on the stage of a polarizing microscope; there are no 'extinction' (minimum intensity) positions. The reason for this is demonstrated geometrically in Fig. 2. OPl_1 and OPl_2 are the 'slow' vibration directions of the plates, the latter being that for the upper plate, that is the one nearer to the analyser. OB is the bisectrix of the angle between these directions. OP is the vibration direction and amplitude of the light from the polarizer. Since $\delta = 180°$, or $(n \times 360°) + 180°$, the light emerging from each plate must be linearly polarized, and have the same amplitude as that coming from the polarizer. By applying the ordinary construction we find that the vibration vectors of the light emerging from the lower and upper plates are OL and OH respectively, and $OH = OL = OP$. It can readily be proved that the direction of OH is independent of the angle $BOP(\alpha)$, and dependent only on the angle Pl_2OPl_1 (2θ). The amplitude of the component which passes the analyser, OA', therefore remains constant as the plates are rotated in unison.

If the plates be interchanged without changing the angle 2θ, so that OPl_1 now refers to the upper plate, the vibration direction and amplitude of the light emerging from this plate is found to be OH', which makes the same angle φ with the analyser vibration direction as OH, and thus gives the same amplitude OA' for the component which passes the analyser. (In conformity with this result, the expressions given above take no account of which plate is on top.)

By rotating the analyser so that its vibration direction becomes perpendicular to that of the light emerging from the upper plate extinction results, and this extinction is not relieved when the plates are rotated in unison. Thus if OH is the vibration direction of the light coming from the top plate, extinction is obtained by rotating the analyser through the angle $(90 - \varphi)$ to OE. This angle is related to 2θ as follows:

$$\sin(90 - \varphi) = \cos\varphi = OA'/OH = \sin(4\theta) \qquad (4)$$

(The last step in this relationship follows from equation (3), which gives the relative intensity, that is $(OA'/OP)^2$, as $\sin^2(4\theta)$. Thus $OA'/OP = OA'/OH = \sin(4\theta)$.) Equation (4) has two solutions, since 4θ can be either $(90 - \varphi)$, or $(90 + \varphi)$, the sines of which are equal.

Extinction can also be obtained by rotating the polarizer through the angle $(90 - \varphi)$, but in the opposite direction, thus bringing OH perpendicular to the analyser vibration direction.

The above case can only apply exactly for one wave-length with any given pair of plates for which it applies at all, but if this wave-length (which we will now refer to as μ_{180}) is near to the middle of the spectrum, a good approximation to the characteristic effects which have been described is obtained even when white light is used. This can be readily demonstrated by superposing cleavage strips of mica, for each of which μ_{180} is in the yellow or yellow-green, on the stage of a polarizing microscope which is illuminated with white light. On rotating the stage, no positions of minimum intensity can be distinguished (at least with the unaided eye). By turning either the analyser or the polarizer through a certain angle, extinction or near-extinction will be secured, and this will only be slightly relieved on rotating the stage. The reason for this behaviour is that the vibration of the light emerging from the upper plate follows a very narrow ellipse for any wave-length within a considerable range on either side of λ_{180}, and the major axis of this ellipse corresponds to much the same vibration direction and amplitude as those of the linearly polarized light of wave-length λ_{180}.

The foregoing has a bearing on the polarization microscopy of cellulosic fibres, the spiral wall structure of which causes them to behave optically in a similar way to systems of superposed plates. When light is passed through a cylindrical fibre of this type, the angle between the 'slow' directions for the front and back walls (2θ in the above treatment) and the thickness presented to the light beam are of course not constant across the fibre, so that each vertical longitudinal section shows different optical effects. Flattened, ribbon-like fibres, such as those of dry cotton, however, approximate very closely to systems of two flat plates, except where they are twisted. Taking cotton, in which the spiral angle is considerable (*ca.* 30° with respect to the fibre axis), as an example, the following observations may be made. In immature fibres the walls are very thin and δ is very much less than 180°. Between crossed polars such a fibre shows well-defined minima of intensity when its axis is parallel to the vibration directions of the polars, and it also behaves towards compensators as though its axis were a 'slow' direction of vibration. Among the thicker fibres of mature cotton, however, some will be found which show all the properties described above for the case $\delta = 180°$, or approach this behaviour very nearly, at least along portions of their length. The behaviour of such fibres towards compensators is quite ambiguous, because over a large part of the spectrum the emergent light is approximately linearly polarized, with a vibration direction which is little affected by the position of rotation of the stage, as explained above.

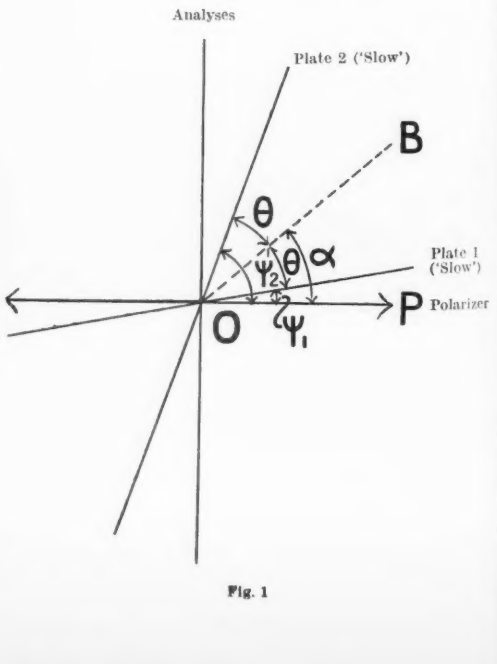

Fig. 1

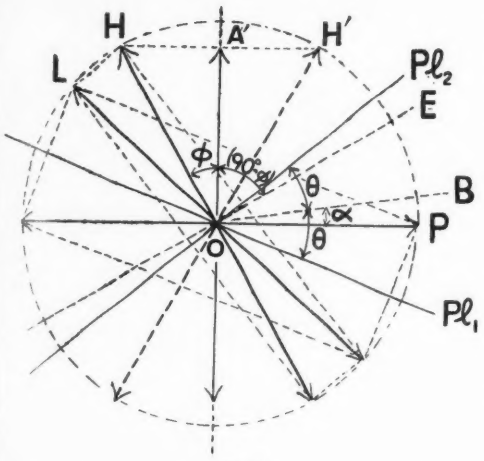

Fig. 2

By means of equation (4) it should be possible to obtain at least approximate values of the spiral angle from measurements of the angle $(90 - \varphi)$ made at the wave-length λ_{180}. This wave-length can be estimated roughly with the aid of suitable filters, or more accurately by means of a monochromator, as being that at which the closest agreement with the theoretical behaviour for the case $\delta = 180°$ is obtained.

This case and its consequences are not dealt with in any of the publications on fibre microscopy with which I am familiar.

N. H. Hartshorne

Department of Inorganic and
Structural Chemistry,
The University,
Leeds.
April 13.

Birefringence of Montmorillonite Complexes

During a study of the optical properties of montmorillonite aggregates in salt solutions[1], some interesting preliminary observations were made on various aromatic complexes. These observations have now been followed up with the view of extending the use of optical data in characterizing clays.

The structures of various aromatic complexes of montmorillonite have been inferred from spacing measurements and one-dimensional Fourier synthesis[2]. The monolayer complexes could be grouped into two classes, those where the plane of the ring was parallel to that of the silicate sheet (type *A*) and those where it was perpendicular (type *B*). Clearly, because the polarizability of the aromatic ring is usually much greater in the plane of the ring than perpendicular to it[3], the preferred orientation of the interlayer molecules in aromatic complexes should profoundly affect the apparent birefringence of the mineral. Thus, in type *B* complexes, the effect of the interlayer molecules would be expected to reduce the strong negative birefringence of the silicate layers and even make some aggregates optically positive. In contrast, type *A* complexes would be expected to be strongly negative. These expectations were strikingly confirmed when the birefringence of the nitrobenzene complex (type *B*) was found to be 0·003 (negative) as compared with 0·029 (negative) for the unexpanded mineral. An even larger effect was to be expected with quinoline, which is more anisotropic than nitrobenzene[4], and the orientation of the interlayer molecules is such as to increase greatly the polarizability of the complex perpendicular to the silicate sheets[4]. Measurement of its birefringence showed it to be 0·02 (positive). In contrast, type *A* complexes were found to be strongly negative, for example, pyridinium montmorillonite (type *A*) was 0·024 (negative).

These large birefringence changes obtained with montmorillonite not only confirm the proposed orientation of the interlayer molecules, but could be used to characterize clays in the same way as glycol and glycerol are used in X-ray diffraction analysis. For example, rapid assessment of clays for montmorillonite minerals is possible by measuring the changes in birefringence of aggregates on immersion in quinoline solutions. Where montmorillonite predominates, the optical sign is changed after treatment. Again, clays known to be homogeneous, but partially expanding and giving a complex X-ray diffraction pattern, have been rapidly and simply evaluated in terms of the percentage of expanding layers, from the change in birefringence in different solvents. When evaluation has been possible from X-ray results[5], the agreement between the two methods has been excellent.

The preliminary part of this work was done while I held a Royal Society Exchange Fellowship, 1957–58, with the Academy of Sciences, U.S.S.R.

R. Greene-Kelly

Rothamsted Experimental Station,
Harpenden, Herts.
May 12.

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Electron Paramagnetic Resonance at 4·2° K. of λ-Irradiated Polymethyl Methacrylate and Polymethacrylic Acid

The electron paramagnetic resonance spectrum given by polymethyl methacrylate after high-energy irradiation at room temperature consists of five lines, about 23 gauss apart, with intensities in approximately the ratios 1 : 4 : 6 : 4 : 1, with a weaker intermediate pattern of four lines, both closely centred on the electron spin g factor of 2·00[1,2]. Since this spectrum is also given by free radicals trapped during the addition polymerization of methyl methacrylate[3–5], it has been postulated that it arises from trapped propagating radicals of structure, $—CH_2—\dot{C}(CH_3)CO_2CH_3$, the detailed explanations involving the exact conformation of these radicals[2,4,6]. Both of the explanations put forward by Symons[4,6] require that the methyl group bonded to the 'radical' carbon atom rotates rapidly, so that its three protons interact equally with the unpaired electron. If one of these

explanations is correct, the hyperfine structure of the spectrum should alter when the temperature is lowered sufficiently. The rotation of the methyl group might change to a torsional oscillation, thus destroying the equivalence of the three methyl protons. If however the rotation remains free, at a temperature where only the lowest rotational level is populated, symmetry conditions will govern the occupation of the nuclear spin levels.

Laboratory-prepared samples of polymethyl methacrylate and polymethacrylic acid were gamma-irradiated at room temperature with doses of about 10^7 r. using a cobalt source. Their spectra were measured at 77° K. and 4·2° K. with a 3,000 Mc./s. spectrometer using low amplitude 100 c./s. magnetic field modulation with phase detection to give the first derivative of the absorption spectrum[7]. The samples were contained in Dewar vessels inserted into the microwave cavity. At 77° K. both polymers gave the well-known spectrum (Fig. 1). The spectra at 4·2° K. (Fig. 2) also consist of nine lines with essentially the same spacings, centred on $g = 2{\cdot}00$. However, a marked change in the relative intensities of the lines has occurred. Polymethacrylic acid showed no power saturation at 4·2° K.; but when the temperature was further lowered, broadening of the individual hyperfine components occurred at high microwave power. At 4·2° K. the polymethyl methacrylate spectrum was considerably broadened at high microwave power, and the spectrum shown was obtained at very low microwave power. Owing to overlap it is difficult to make accurate estimates of the relative intensities of the hyperfine components. The absorption-curves obtained by graphical integration were fitted by patterns with relative intensities of approximately 1 : 2 : 3 : 4·5 : 5 : 4·5 : 3 : 2 : 1, for polymethyl methacrylate and 1 : 1·7 : 2·3 : 2·5 : 2·5 : 2·5 : 2·3 : 1·7 : 1, for polymethacrylic acid. The individual line widths are similar for all three spectra, and the decreased resolution at 4·2° K. arises from the change in relative intensities.

The total wave function of the radical must be antisymmetric to exchange of nuclei, and if it were behaving as a free rotator with only the lowest level occupied, only antisymmetric nuclear spin functions would be allowed[8]. Those states in which all nuclei are aligned either with or against the electron spin would be forbidden and the outermost hyperfine components would not be present. It is clear that this effect is not operating here.

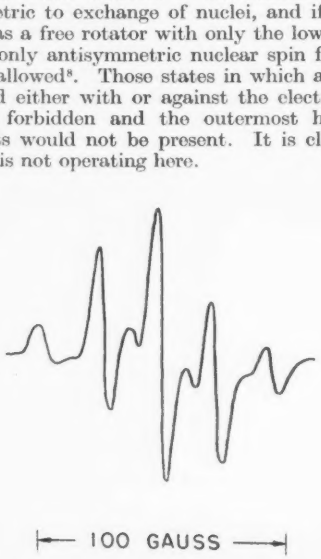

Fig. 1. First derivative of electron paramagnetic resonance spectrum at 77° K. of γ-irradiated polymethyl methacrylate

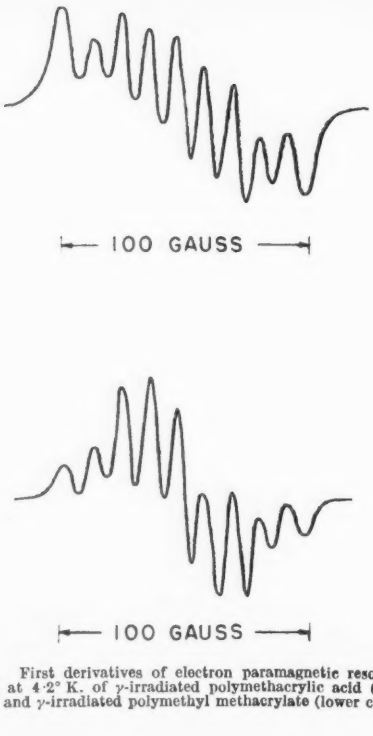

Fig. 2. First derivatives of electron paramagnetic resonance spectra at 4·2° K. of γ-irradiated polymethacrylic acid (upper curve) and γ-irradiated polymethyl methacrylate (lower curve)

Explanations of these spectra based on non-rotation of the methyl group have been attempted. Since the total hyperfine splitting is unchanged, the sum of the coupling coefficients of the three methyl protons must be unchanged. These coupling coefficients must be multiples of the line spacing (11·5 gauss). There are two possible cases, corresponding to two positions of the methyl group which have one proton either in line with, or orthogonal to, the 'radical' carbon atom p orbital. When these are taken with either of Symons's suggestions regarding the coupling of the methylene protons[4,6], nine line spectra with the observed spacings are predicted, but it is not possible to obtain even an approximate fit to the observed intensity ratios.

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Derick W. Ovenall

Department of Physics,
Duke University,
Durham, North Carolina.

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CHEMISTRY

Electron Spin Resonance and Divalency of Some Dithiocarbamates of the Coinage Metals (Cu, Ag, Au)

In a previous paper[1] one of us reported an investigation of the N,N-dialkyldithiocarbamates of the univalent coinage metals, and in another[2] the reaction of the compounds in question with the corresponding thiuram disulphides. Several of these compounds are not only of significant theoretical interest but they also play an important part in several branches of practical chemistry (for example, as ultra-accelerators in rubber vulcanization, antioxidants in lubricants, in medicine for treatment of chronic alcoholism, etc.).

As divalent copper, silver and gold compounds all would be paramagnetic with electron configurations $3d^9$, $4d^9$, $5d^9$ respectively, it is possible to infer the existence of this oxidation state from a study of the electron spin resonance absorption spectra. This investigation gives, among other things, the first proof of the existence of the divalent oxidation state of gold.

X-ray investigations by Hesse[3] and Peyronel[4] show that the copper compounds, $(R_2NCS_2)_2Cu$, form square planar complexes. It seems very likely that the corresponding silver and gold complexes have an analogous structure.

Fig. 1 shows typical spectra obtained from solutions of copper, silver and gold complexes. The spectra of the ethyl-, *iso*propyl- (Fig. 1*a*) and methyl-phenyl copper compounds are almost identical and have a g value of 2·046. The four hyperfine lines vary in width. This is typical for copper complexes and arises from insufficient averaging of the anisotropic resonance structure[5]. The high-field line is so narrow (width about 4 gauss) that the hyperfine structure of the two copper isotopes copper-63 and copper-65 is resolved. The hyperfine separation of copper-63 is $7{\cdot}4 \times 10^{-3}$ cm.$^{-1}$.

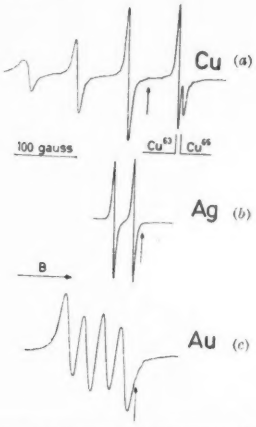

Fig. 1. Derivatives of electron spin resonance absorption curves recorded at room temperature. Microwave frequency about 9,500 Mc./s. The arrows indicate the resonance field for free electrons. Solvent, benzene. (*a*) [(*iso*-$C_3H_7)_2$ $NCS_2]_2$ Cu; (*b*) [(*iso*-$C_3H_7)_2$ $NCS_2]_2$Ag; (*c*) [(*iso*-$C_3H_7)_2$ $NCS_2]_3$Au

If silver(I) N,N-diakyldithiocarbamates are mixed with the corresponding thiuram disulphides dissolved in benzene or chloroform, the solution immediately turns blue[2]. The colour is most probably due to a divalent silver compound; the reaction may then be written schematically as:

$$RSAg + \tfrac{1}{2}RSSR \rightleftharpoons RSAgSR \qquad RS = \begin{matrix} R' \\ \diagdown \\ NCS_2 \\ \diagup \\ R' \end{matrix}$$

The electron spin resonance spectra of these solutions (Fig. 1*b*) definitely confirm the divalency of silver. In the same environment the general features of the electron spin resonance spectra of divalent copper and silver should be the same, and this was found to be so in an investigation by Bowers[6]. We obtained a doublet due to the hyperfine interaction of the two naturally abundant isotopes of silver, both with nuclear spin of $\frac{1}{2}$. If the spectra are expanded it is just possible to see the hyperfine structure of the individual isotopes, silver-107 and silver-109 (nuclear magnetic moments $-0{\cdot}113$ and $-0{\cdot}130$ nuclear magnetons, respectively). The line-width is approximately 2·5 gauss. The widths of the two hyperfine lines differ slightly, and this can be explained in the same way as the line-width variation of the copper compounds. The g value is 2·019 and the mean hyperfine separation is $2{\cdot}7 \times 10^{-3}$ cm.$^{-1}$. The similarity of the g values of these and the corresponding copper compounds also indicates that the structures of the complexes are the same.

From chemical evidence the reaction between the gold(I) N,N-dialkyldithiocarbamates and the corresponding thiuram disulphides may be written schematically as follows[2]:

$$RSAu^{I} + RSSR \rightleftharpoons (RS)_3Au^{III} \qquad RS = \begin{matrix} R' \\ \diagdown \\ NCS_2 \\ \diagup \\ R' \end{matrix} \qquad (1)$$

The reaction is rather slow. In a typical electron spin resonance experiment *RS*Au[I] and *RSSR* dissolved in benzene separately showed no electron spin resonance absorption, but on mixing four lines of equal intensity appeared (Fig. 1*c*). The same spectrum was obtained by dissolving $(RS)_3Au^{III}$ (RS = $(C_2H_5)_2NCS_2$ or (*iso*-$C_3H_7)_2NCS_2$) in benzene. This resonance cannot be due to tervalent gold for the following reasons. No complex of the tervalent coinage metals (except CuF_6^{3-}) has been found to be paramagnetic. Also we have made preliminary static susceptibility investigations of some gold(III) N,N-dialkyldithiocarbamates (both solid and in solution) which indicate that these compounds are diamagnetic. Furthermore, we could not detect any electron spin resonance absorption of the solid compounds. We also found by comparison with copper compounds that the intensity of the resonance absorption of the gold(III) compounds dissolved with an excess of thiuram disulphide (to prevent the reversal of reaction 1), was at most 1 per cent of what one would expect if the resonance was due to tervalent gold. The electron spin resonance absorption of the dissolved gold(III) complexes decreased on adding more disulphide, which should, however, increase the gold(III) concentration. Similarly, if disulphide was added to a solution containing a large excess of the

gold(I) compound, the resonance signal stayed constant even though the gold(III) concentration was at least doubled.

As it is impossible to explain the four equally intense lines in terms of hyperfine structure of free radicals we conclude that the resonance lines originate from divalent gold. The resonance data themselves give strong evidence for the existence of divalent gold compounds. The g value of the gold(II) complex is 2·040 which is close to those of the copper and silver compounds, and the hyperfine structure is consistent with the nuclear spin of gold-197 which is 3/2. The hyperfine separation is $2{\cdot}8 \times 10^{-3}$ cm.$^{-1}$.

Further experiments including single crystal investigations are planned. We also hope to be able to clarify why the resonance line-width of the gold compounds is greater than that of the copper and silver compounds.

We wish to thank Profs. A. Fredga and K. Siegbahn for their interest in our work.

Tore Vänngard
Stig Åkerström
Institutes of Physics and Organic Chemistry,
University of Uppsala.
May 1.

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Phototautomerization of Cytosine Derivatives on Ultra-violet Irradiation[1]

Unstable products were formed from certain cytosine derivatives on ultra-violet irradiation. These products had a new band at ~240 mμ and lacked the characteristic ~270 mμ maxima of cytosine derivatives. The products were not only reconstituted to their original compounds in the presence of acid and base but also spontaneously reconstituted themselves on standing, as indicated by the reversion of the ultra-violet spectra[2]. Therefore, in these respects the cytosines differ from the uracils[1,3].

Because of the phenomenon of reversibility, investigators had classified cytosine derivatives and uracil derivatives together as one group from the point of view of photochemical behaviour[2]. However, the electronic configurations of the two types are distinctly different. Since in aqueous solution, 4-hydroxy groups exist predominantly in the ketonic form (II) and the 4-amino group in the amino form (I), the uracils have exocyclic double bonds (C=O) at C^4 while the cytosines have endocyclic double bonds (N=C)[3]. Consequently, the photochemical pathway of cytosines might be altogether different from that of uracils.

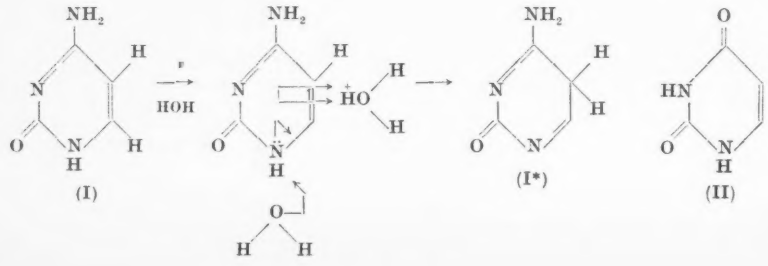
Indeed, Shugar *et al.*[2] in their excellent study of cytosine derivatives have shown that irradiation, whether carried out in acid (pH 1–2), in alkaline (pH 9–11), or in neutral solutions produced similar photoproducts, which spontaneously reconstitute on standing. Both Shugar *et al.* and Sinsheimer[2] postulate the formation of photoproducts involving the addition of water. Since the photoproducts which they postulate are known to be stable only around neutrality, the existence of these molecules is most unlikely at either an extreme alkaline or acid pH during or after irradiation. If these products were actually formed, the decrease of optical densities during irradiation should have been similar to that seen upon thymine irradiation[4]. However, irradiation of cytosines at either an extreme alkaline or acid pH still gave reversible products instead of irreversible products, thus leading us to the conclusion that the unstable product probably is not a hydrated cytosine.

Irradiation of cytosine in buffered (pH 7) solution did not give a reversible product. However, irradiation in non-buffered solution gave a reversible product. Similar reversible products were produced from cytidine and cytidylic acid in either buffered or non-buffered solution. This indicated that when N^1H (N^3H) is not substituted, the salt effect from the buffer suppresses the formation of the reversible product. Therefore, it suggested that $N^1(N^3)$ is probably involved in this photochemical change. (Synthetic $N^1(N^3)$ substituted cytosine derivatives behave similarly to that of cytosine. Using structural isomers we are now investigating the basis of this discrepancy.)

The decrease of optical densities at 270 mμ with a simultaneous increase at 240 mμ does not necessarily indicate the formation of dihydro derivatives, because these reduced compounds do not exhibit $\varepsilon_{max.}$ at any wave-length longer than 230 mμ [5].

On close examination of the absorption spectrum at neutral pH there is apparently a shoulder at ~240 mμ besides the principal ~270 mμ maxima. Therefore, the so-called new maximum at ~240 mμ probably represents the increase of the optical density at the shoulder for that particular component structure.

From the above evidence, a tautomerization by irradiation seemed most likely to us. Indeed such an unstable tautomer (I*) as shown involves $N^1(N^3)$ in the tautomerization. It is not a dihydro derivative resulting from a hydration product of cytosines. The shift from 270 mμ to 240 mμ is probably due to the change of a straight conjugation to a cross conjugation of the chromophore. The higher extinction at 240 mμ is probably due to the separation of charges in a molecule. Furthermore, barbital derivatives, which have chromophores similar to that of the tautomer, have the $\varepsilon_{max.}$ at 240 mμ [6]. In the dark the unstable tautomer should revert to their most stable form, having the original spectra.



In order to demonstrate this tautomerization or isomerization, cytosine, cytidine and cytidylic acid were irradiated respectively both in buffered and non-buffered solutions. It will be evident from Figs. 1 and 2 that

isosbestic points are present indicating that isomerization must have occurred[7]. Irradiation of cytosine in buffered solution did not give an isosbestic point; therefore an irreversible product was formed. The spontaneous isomerization rather than the reversibility of the compounds of spectra in acid and base was the most interesting phenomenon about these observations. It indicates that an excited molecule can result from the absorption of photic energy and that this energy can be released slowly in another form, possibly available for chemical changes, without other influences, such as enzymes, heat, acidity, etc. The apparent half-life of the irradiated cytosine, cytidine and cytidylic acid are 50, 30 and 200 min., respectively.

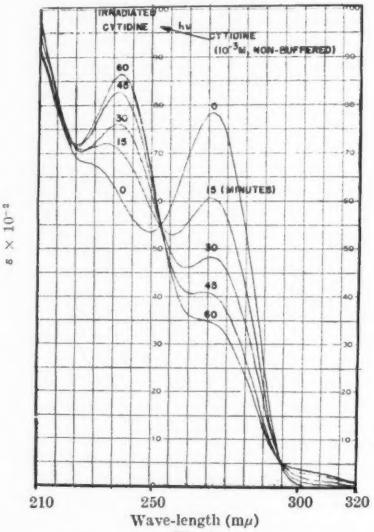


Fig. 1

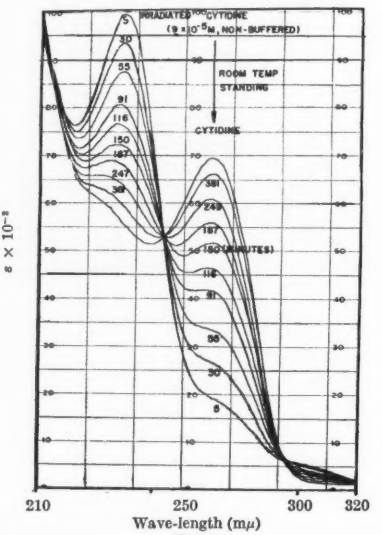


Fig. 2

The above results raise the question of the possible part that this phenomenon might play in biological systems.

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SHIH YI WANG

Physiology Department,
Tufts University School of Medicine,
Boston 11, Massachusetts.

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Isotopic Composition of Boron

IN a recent communication[1] it was concluded that a boron 11/boron 10 ratio of 4·00 approaches the true natural abundance ratio much more closely than the presently accepted value of 4·31. This value of 4·00 had been obtained from the mass spectra of boron hydrides and other volatile compounds.

Using a Metrovic mass spectrometer designed for the surface ionization of solids from a filament source and working with borax, we have obtained consistent results within the range 4·06–4·09 for the boron 11/boron 10 abundance ratio.

D. C. NEWTON
A. C. TYRRELL
J. SANDERS

The Plessey Co., Ltd.,
Caswell,
Towcester,
Northants.
June 3.

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Stoichiometry of Bismuth Telluride and Related Compounds

BISMUTH telluride, bismuth selenide and antimony telluride are being actively studied as semiconductors for thermoelectric cooling[1]. After purification by zone melting these materials do not exhibit intrinsic properties[2]. C. B. Satterthwaite and R. W. Ure[3] have shown by electrical measurements that in the case of bismuth telluride there is a slight difference between the composition corresponding to the maximum of the liquidus curve and the stoichiometric composition. Electrical properties are sensitive to physical imperfections and their interpretation in terms of chemical composition is thus open to criticism[4].

By using a sensitive method of differential thermal analysis we have found it possible to determine the composition corresponding to the maximum in the liquidus curve. The principle of this method is the use of the fact that for this composition the solid melts congruently whereas, for slightly different compositions it yields, after a suitable heat treatment, a mixture of two solid phases having different isothermal transition points.

Bismuth telluride containing excess tellurium forms an eutectic[5] melting at 413° C., and excess bismuth gives rise to a peritectic reaction[6] at 540° C. Bismuth

selenide[7] with excess selenium is characterized by a monotectic transition at 605° C., associated with an eutectic isotherm at about 217° C.; with excess bismuth a peritectic phase appears at 605° C. The phase diagram of the system antimony–tellurium is characterized by an eutectic with excess tellurium at 400° C. and another eutectic with excess antimony[8] at 545° C.

The signals given by the melting of eutectic phases, monotectic transitions or peritectic reactions are proportional to the quantities of the individual phases

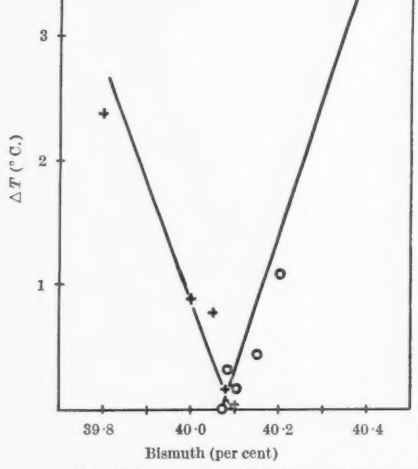

Fig. 1. System Bi/Te: +, Amplitudes of eutectic signals (quenched samples); ○, amplitudes of peritectic signals (annealed samples)

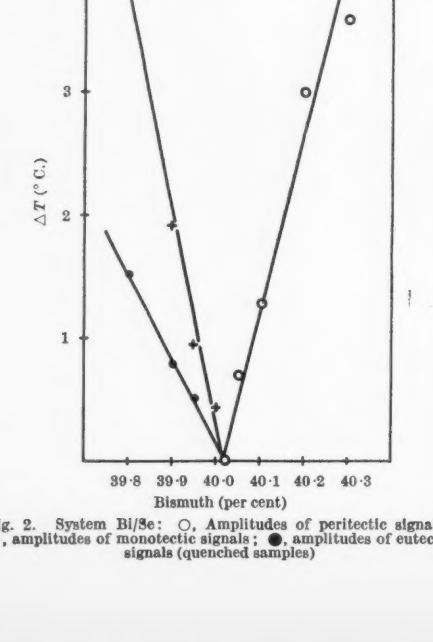

Fig. 2. System Bi/Se: ○, Amplitudes of peritectic signals; +, amplitudes of monotectic signals; ●, amplitudes of eutectic signals (quenched samples)

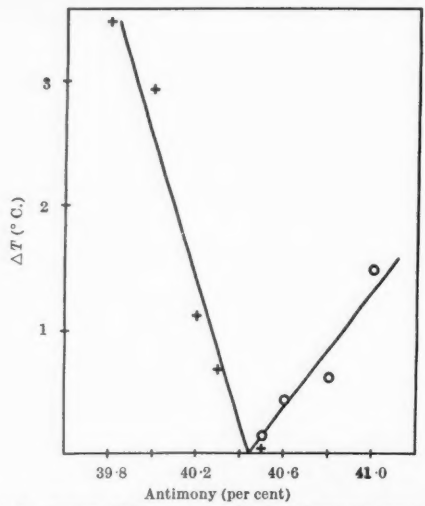

Fig. 3. System Sb/Te: +, Amplitudes of eutectic signals at 400° C.; ○, amplitudes of eutectic signals at 545° C. (quenched samples)

present and may be used as a measure of their concentrations. In the case of the eutectics, the samples are quenched from the liquid state in order to avoid the formation of a solid solution; in the other case, the samples are carefully annealed at a suitable temperature in order to carry the reaction as nearly as possible to completion.

The results of the experiments are given in Figs. 1, 2 and 3. It is evident that the congruent compositions for these three systems is:

Bismuth telluride: Bi 40·065/Te 59·935 ± 0·015
Bismuth selenide: Bi 40·02/Se 59·98 ± 0·02
Antimony telluride: Sb 40·40/Te 59·60 ± 0·05

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G. Offergeld
J. van Cakenberghe
European Research Associates,
95 rue Gatti de Gamond,
Brussels.

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Determination of Magnesium in Blood Serum by Atomic Absorption Spectroscopy

The present lack of detailed knowledge of the function of magnesium in the human body is due partly to the lack of rapid and reliable methods for its routine estimation in small quantities of biological materials. Recently, Hunter[1] has devised a method for determining calcium and magnesium in blood serum by titration with murexide and with 'Eriochrome T'. It uses only 0·2 ml. of serum, but has

the disadvantage of requiring prior removal of protein by coagulation or ashing, and even then the magnesium is estimated indirectly by the difference of the two titrations. Methods for determining magnesium directly normally require removal of calcium also[2–4]. The flame photometer method of Davis[5] requires removal of protein followed by precipitation of the magnesium by 8-hydroxyquinoline.

It has been pointed out[6] that atomic absorption spectroscopy[7] can be used for the determination of magnesium in the ash from blood serum, since interference by sodium, potassium, calcium and phosphate is negligible.

I have recently found that, for the determination of magnesium by the atomic absorption method, ashing is unnecessary, and measurements can be made directly on serum diluted with water containing about 1 per cent of the disodium salt of ethylenediamine tetraacetic acid. The results reported here were mostly obtained on solutions made by diluting 0·25 ml. of serum to 5 ml., but since only 2·5 ml. of solution is required for duplicate determinations and higher dilutions can be used with little sacrifice of accuracy, there is no difficulty in estimating magnesium in as little as 0·05 ml. of serum. Most of the existing methods require at least 1 ml.

The solution was atomized by injection into a 10 cm. air–acetylene flame of the Lundegårdh type, and absorption of the magnesium resonance line at 2852 A. was measured. Calibration was carried out with solutions containing 0·05–0·15 mgm./100 ml. magnesium.

Table 1 shows magnesium contents for samples prepared (*a*) by direct dilution, (*b*) by ashing with nitric acid[8] followed by solution in a few drops of distilled hydrochloric acid and subsequent neutralization and dilution and (*c*) by removal of protein with 0·05 *N* acetic acid[1].

Table 1. MGM. CONTENT OF SERUM (MGM./100 ML.)

Serum No.	Type	(*a*) Direct dilution	(*b*) Ashed	(*c*) Deproteinized filtrate
1	Bovine*	3·56	3·52	3·53
2	Equine	1·75	1·80	—
3	Human	2·57	—	2·50
4	,,	2·22	2·28	—
5	,,	2·43	—	2·58
6	,,	2·50	—	2·66
7	,,	1·70	—	1·63
8	,,	2·22	2·24	2·00
9	,,	1·14	1·04	1·12
10	,,	2·16	1·91	2·10

* Freeze-dried bovine serum ('Chemtrol', supplied by Clinton Laboratories, Los Angeles). The magnesium values are higher than those for most bovine sera.

In view of the chemical and manipulative errors likely to be incurred in the preparation of such dilute solutions (~1 p.p.m.) by methods (*b*) and (*c*) the agreement is considered satisfactory, and the magnesium values obtained by direct dilution are probably more reliable than those obtained by the other methods. Duplicate readings on the same solution seldom differed by more than 2 per cent. Recovery of added magnesium was 100–102 per cent.

Although the present work was carried out with the air–acetylene flame, an air–coal gas flame is also satisfactory, and we are at present developing a very simple instrument which will determine magnesium in blood serum.

A fuller account of the present work will be submitted to *Analytical Chemistry*.

I am indebted to Mr. E. Mason of the Commonwealth Serum Laboratories for a generous gift of horse serum and to Miss B. Splatt of the Biochemistry Department, Royal Melbourne Hospital, for the specimens of human serum.

J. B. WILLIS

Division of Chemical Physics,
Commonwealth Scientific and
Industrial Research Organization
Chemical Research Laboratories,
Melbourne.

June 4.

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BIOCHEMISTRY

Action of Trypsin on α-Carbethoxy-L-lysyl-L-serylglycine and its O-Phosphorylated Analogue

THE occurrence and isolation of phosphorylated peptides from enzymic hydrolysates of casein have already been reported[1,2]. These peptides exhibit unusual resistance to further proteolytic action, a fact which has been correlated with the existence of O-phosphorylated serine residues in their molecules. In order to investigate further the resistance of such peptides to the action of trypsin, certain synthetic peptide-substrates suitable for this enzyme have been tested. Thus α-carbethoxy-L-lysyl-L-serylglycine and α - carbethoxy - L - lysyl - (O - phosphoryl) - L - serylglycine were synthesized as follows.

α-Carbethoxy-(ε-carbobenzoxy)-L-lysine (I) was prepared from ε-carbobenzoxy-L-lysine in a similar manner described for the carbethoxy-*iso*leucine derivative[3]. The oily product thus obtained was coupled by the mixed carboxylic–carbonic anhydride procedure with L-seryl-glycine[4] (II) to give α-carbethoxy-(ε-carbobenzoxy)-L-lysyl-L-serylglycine (III) in 50 per cent yield, melting point 204° C. Analysis calculated for $C_{22}H_{32}N_4O_9$, N 11·2; found, N 11·1. When α-tosyl-(ε-carbobenzoxy)-L-lysine, melting point 115–117° C., or the corresponding α-benzoyl derivative, melting point 110° C., were used, the coupling did not proceed satisfactorily, probably due to steric hindrance[5]. Hydrogenolysis[6] of III produces α-carbethoxy-L-lysyl-L-serylglycine (IV), $[\alpha]_D^{25}$—28·9° (*c* 0·76 in water). Analysis calculated for $C_{14}H_{26}N_4O_7$. $2H_2O$, N 14·1; found, N 13·9. Compound II was treated with benzyl alcohol in the presence of *p*-toluenesulphonic acid to give L-serylglycine benzyl ester *p*-toluenesulphonate (V) in 90 per cent yield, melting point 180° C. Analysis calculated for $C_{19}H_{24}N_2O_7S$, N 6·5; found, N 6·2. The ester V was condensed with I by the anhydride procedure to afford α-carbethoxy-(ε-carbobenzoxy)-L-lysyl-L-serylglycine benzyl ester (VI) in 50 per cent yield, melting point 185–186° C., $[\alpha]_D^{25}$—17·6 (*c* 1·5 in acetic acid). Analysis calculated for $C_{29}H_{38}N_4O_9$, C 59·36, H 6·52, N 9·7; found, C 59·4, H 6·7, N 9·5. To eliminate the side reaction with the hydroxyl group of serine, the ester V was dissolved in tetrahydrofuran/water (5 : 1) in the presence of two equivalents of triethylamine and then added to the anhydride solution.

Hydrogenolysis of VI produces IV with the same optical rotation. Coupling of I with V by the carbodiimide method gave VI with melting point 185–186° C. Phosphorylation of VI with diphenylphosphoryl chloride[7] in anhydrous pyridine resulted in the production of an amorphous product, which analysis suggested was a mixture of O-phosphorylated and unphosphorylated peptide derivative, although 50 per cent excess of the chloride was used. Compound VI dissolved in anhydrous pyridine and recovered after 2 hr., showed almost no change of its optical rotation.

Removal of protecting groups from the amorphous product by hydrogenolysis in the presence of palladium on charcoal, gave a mixture in which the monophenyl derivative predominated. Final removal of this was then attempted by further hydrogenolysis in the presence of platinum as the catalyst. Following paper electrophoresis in pyridine–acetate buffer, *p*H 5·5, revealed three ninhydrin-positive spots. The most intense and anodically fast moving one corresponded to the phosphorylated peptide. The desired product α-carbethoxy-L-lysyl-(O-phosphoryl)-L-serylglycine (VII), $[\alpha]_D^{20}$—23·6° (*c* 1 in water), was isolated by anion-exchange chromatography (Strid, L., unpublished work). Paper electrophoresis revealed one spot. Analysis calculated for $C_{14}H_{27}N_4O_{10}P$, N 12·6, P 7·0; found, N 12·05, P 7·3.

Compounds IV and VII were respectively incubated with trypsin in 0·2 *M tris*(hydroxymethyl) aminomethane hydrochloride buffer, *p*H 8·25, at 25° C. Qualitative analysis of hydrolysis products, on the other hand, was carried out by paper chromatography in butanol/acetic acid/water (4 : 1 : 5) system. The course of reaction was also followed by colorimetric analysis with ninhydrin reagent[8]. To this end, aliquots were withdrawn at different time intervals, mixed with 0·2 *M* citrate buffer, *p*H 5, at 5–6° C. and then analysed.

As is indicated in Fig. 1, a phosphoryl residue attached to the hydroxyl group of serine renders the lysylserine peptide bond resistant to tryptic action. Paper chromatography of the incubation mixture of VII with trypsin also supported this conclusion. On the other hand, the incubation mixture of IV revealed two spots corresponding to α-carbethoxy-L-lysine and L-serylglycine respectively.

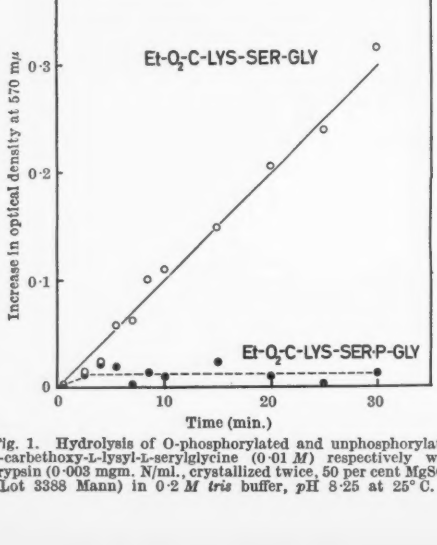

Fig. 1. Hydrolysis of O-phosphorylated and unphosphorylated α-carbethoxy-L-lysyl-L-serylglycine (0·01 *M*) respectively with trypsin (0·003 mgm. N/ml., crystallized twice, 50 per cent $MgSO_4$, Lot 3388 Mann) in 0·2 *M tris* buffer, *p*H 8·25 at 25° C.

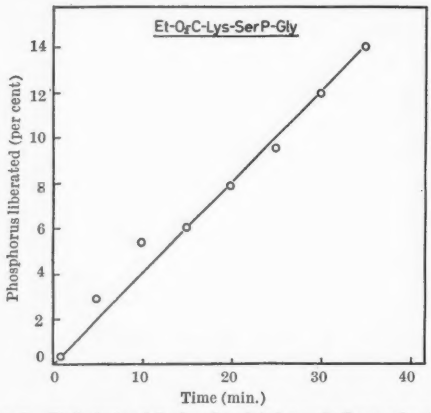

Fig. 2. Hydrolysis of O-phosphorylated L-carbethoxy-L-lysyl-L-serylglycine (0·01 *M*) with intestinal alkaline phosphatase (0·1 mgm./ml., crude preparation. Lot 1105 Mann)

The effect of alkaline phosphatase on α-carbethoxy-L-lysyl-(O-phosphoryl)-L-serylglycine at *p*H 9·5 (0·1 *M* triethylamine–carbon dioxide buffer) at 25° C. is shown in Fig. 2. The amount of phosphorus liberated was determined by the modified method of Beerenblum and Chain[9].

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D. Theodoropoulos*
H. Bennich
G. Fölsch
O. Mellander

Department of Medical Biochemistry,
University of Gothenburg.

* Swedish Medical Research Council Postdoctoral Fellow.

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A Micromethod for the Polarographic Determination of Serine

The serological behaviour of red blood cells is known to be altered by treatment with dilute solutions of potassium periodate. There is also some evidence that during the interaction of potassium periodate solutions with red blood cells, measurable quantities of periodate ion are consumed[1]. While investigating the consumption of periodate ions by red blood cells, a method for the determination of relatively small amounts of serine was developed.

Malaprade[2] has described how compounds containing adjacent hydroxyl groups as well as hydroxy-amino-acids are oxidized by periodate ion. Based on this observation, several methods have been devised for the determination of serine by means of the periodate ion[3–5]. These methods, however, including that of Boyd[4] and Bambach[5] based on the polarographic determination of formaldehyde formed by the action of the periodate ion and separated by

distillation—are rather cumbersome and the smallest amounts of substance measurable exceed those involved in the phenomenon investigated by us. Zuman[6] pointed out recently, that the capacity of the compounds—including serine—mentioned above to remove periodate ions from solution might be followed polarographically, thus permitting a closer study of the kinetics of the processes.

Taking into account the peculiar features of the interaction of the periodate ion with red blood cells and the probable amounts of the substances involved, the following simple procedure, based on the measurement of the decrease in the IO_4^--wave due to the action of serine, has been used by us.

2·8 ml. of a 0·85 per cent solution of sodium chloride, containing 0·01 per cent of gelatine as maximum suppressor and 0·2 ml. of a 2×10^{-3} *M*

Fig. 1. Polarogram showing the periodate consumption of serine. I, 307 μgm./ml. potassium periodate II, III, IV, V, 16·3, 27·2, 38·0 and 48·9 μgm./ml. serine added. Applied voltage : 2 V. Galvanometer sensitivity : 1/40. Wave heights measured from the galvanometer zero-line : 72, 59, 49, 43 and 35 mm., respectively

solution of potassium periodate were measured into each of two polarographic cells of convenient size and form. To one of the cells 0·02–0·08 ml. of an aqueous solution $1{\cdot}4 \times 10^{-2}$ *M* serine (Fluka p.a.) was added by means of a micro-pipette, the final concentration of serine thus being 10–40 μgm./ml. The solutions were allowed to stand for 2½ hr. at room temperature. After removing dissolved oxygen by bubbling nitrogen through the cells for 30 min., and using as external anode a mercury–mercurous sulphate electrode in saturated sodium sulphate solution, the polarograms of the two solutions were recorded with the aid of a Heyrovský polarograph, model *V*-301*b*. (Polarograms were taken at room temperature, 10–22° C. ; $t = 2{\cdot}5$ sec. ; $m = 3$ mgm. sec.$^{-1}$; $m^{2/3}\,t^{1/6} = 2{\cdot}42$ mgm.$^{2/3}$ sec.$^{-1/2}$.)

Making use of a calibration curve previously constructed the concentration of serine was obtained from the difference in amplitude of the IO_4^--wave recorded with and without serine respectively.

The accuracy of the polarographic method described is 5–10 per cent (depending on the range of concentration of serine) which can be considered for our present purpose to be satisfactory.

J. Ladik
I. Szekács

State Institute of Hygiene,
Department of Biochemistry and
Isotope Research,
Budapest, IX.

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Macromolecular Synthesis in Bacterial Recovery from Ultra-violet Light

Doudney and Haas[1] reported a marked increase in survival ('recovery') of *Escherichia coli* strain *B* when incubated following exposure to ultra-violet light in a nitrogen-free medium. This effect is similar to that described by Roberts and Aldous[2] in 1949. In 1958, these workers[3] reported that chloramphenicol, added to *E. coli* strain *B* cultures after 30 min. incubation following exposure to ultra-violet radiation, promotes a marked increase in survival. However, if the chloramphenicol is added immediately following irradiation, no increase in survival is observed with incubation. The results suggested that protein synthesis is necessary to bacterial recovery initially but is detrimental with subsequent incubation. Recently Gillies and Alper[4] confirmed these basic findings with ultra-violet radiation and extended them to X-rays. This communication presents evidence which relates bacterial recovery to metabolic repair of the mechanism for the synthesis of deoxyribonucleic acid after damage by irradiation.

The basic procedures used in these experiments were as follows : 50-ml. portions of minimal medium[1] were inoculated from a 24-hr. agar slant culture of the organism under investigation and incubated for 15·5 hr. at 37° C. under aeration. The cells were centrifuged out and resuspended in fresh media and the incubation continued for 3 hr. The cells were then centrifuged out again and resuspended in fresh warm minimal medium and the turbidity adjusted to yield approximately 10^8 colony-forming cells per ml. The suspension in 5-ml. lots was then exposed to ultra-violet radiation as previously described[1]. Supplements were then added to the cells immediately as indicated in the tables and the incubation continued on a shaker for the indicated interval. Samples of the proper dilution were then plated on to Difco *EMB* agar and the plates incubated for 3 days prior to counting colonies. Ribonucleic acid[5], deoxyribonucleic acid[6] and protein[7] were determined using the separation procedure of Ogur and Rosen[8]. In the case of the auxotrophic strains, the minimal medium was supplemented as follows : *B*39, uracil, 0·05 mgm. per ml. ; *WP*2, DL-tryptophan, 0·2 mgm. per ml. ; 15*T*, thymine, 0·05 mgm. per ml.

Table 1. Effect of Blockage of Ribonucleic Acid and Protein Synthesis on Reparation of Deoxyribonucleic Acid Synthesis following Exposure to Ultra-violet Light

Organism and treatment*	Relative amount of deoxyribonucleic acid with incubation time (min.)					
	20	40	60	80	100	120
E. coli strain *B*						
Unexposed	1·3	1·6	2·0	2·8	4·4	7·0
UV, 2,395 ergs/mm.^{2}	1·0	1·0	1·3	1·6	2·3	3·3
UV, Chl, 60 min.	1·0	1·0	1·0	1·0	1·3	1·8
UV, 6AU, 60 min.	1·0	1·0	1·0	1·0	1·4	2·0
E. coli strain *WP*2						
Unexposed	1·1	1·4	1·9	2·7	3·4	4·3
UV, 1,675 ergs/mm.^{2}	1·0	1·0	1·0	1·3	1·6	2·1
UV, -tryptophan, 30 min.	1·0	1·0	1·0	1·0	1·2	1·5
UV, -tryptophan, 45 min.†	1·0	1·0	1·0	1·0	1·0	1·0
E. coli strain *B*-39						
Unexposed	1·2	1·6	1·9	2·4	3·1	4·7
UV, 1,449 ergs/mm.^{2}	1·0	1·0	1·1	1·4	2·0	2·9
UV, -uracil, 40 min.	1·0	1·0	1·0	1·0	1·1	1·5
E. coli strain 15*T*						
Unexposed	1·3	2·1	2·7	3·8	4·9	7·4
UV, 960 ergs/mm.^{2}	1·0	1·0	1·4	1·8	2·3	2·8
UV, -thymine, 40 min.	1·0	1·0	1·4	1·9	2·5	2·9
UV, -thymine, 60 min.	1·0	1·0	1·0	1·6	2·1	2·7

* Chl, Chloramphenicol, 20 μgm./ml.; 6AU, 6-aza uracil, 5 mgm./100 ml. Following exposure to ultra-violet the suspensions were incubated in minimal medium with the supplement indicated. The cells were removed from chloramphenicol by rapid centrifugation and resuspension in chloramphenicol free medium. The 6-aza uracil inhibition was reversed by addition of uridine to the medium. The auxotrophic strains were held following exposure to ultra-violet either with or without the appropriate growth supplement. In the case of cells without the required supplement, the supplement was added after lapse of the time indicated.

† Deoxyribonucleic acid synthesis resumed after 150 min. incubation.

Ultra-violet light induces a lag in the synthesis of deoxyribonucleic acid in *E. coli*. An investigation of the metabolic basis of this lag has been carried out, utilizing specific inhibitors of protein and ribonucleic acid synthesis and also auxotrophic strains requiring uracil, thymine or certain amino-acids (Table 1). These findings suggest that ribonucleic acid and protein synthesis (but not deoxyribonucleic acid synthesis) are required for reparation of the deoxyribonucleic acid synthetic system after damage by irradiation with ultra-violet; they are thus in agreement with recent reports[9,10].

Table 2. Effect of Blockage of Ribonucleic Acid and Protein Synthesis on Survival of *Escherichia coli* strain *B* following Exposure to Ultra-violet Light

Ultra-violet dose was 2,395 ergs/mm.². The suspension contained $1{\cdot}4 \times 10^8$ colony forming bacteria per ml. before exposure to ultra-violet. Survivors upon immediate plating following exposure were $6{\cdot}0 \times 10^4$ per ml.

Post-irradiation treatment*		Survivors ($\times 10^4$) per ml. with incubation time (min.) before plating		
Incubation Medium	Added at 40 min.	40	120	160
A. M—N	—	8	43	302
B. M—N + Chl	—	4	3	3
C. M—N + 6AU	—	8	14	31
D. M—N	Chl	7	63	358
E. M—N	6AU	8	40	310
F. M—N + AA	—	7	10	14
G. M—N + AA	Chl	9	68	398
H. M—N + AA + Chl	—	4	4	3
I. M—N + AA	6AU	8	116	480
J. M—N + AA + 6AU	—	7	11	17
K. M—N + AA + Chl	6AU	4	6	7
L. M—N + AA + 6AU	Chl	8	10	10

* M—N, minimal with ammonium sulphate deleted; Chl, chloramphenicol, 20 μgm./ml.; 6AU, 6-aza uracil, 5 mgm./100 ml.; AA, casein hydrolysate, vitamin free, 2 mgm. per ml.

Table 2 shows a marked increase in survival of *E. coli* strain *B* with incubation in minimal medium from which the nitrogen source is deleted. The addition of amino-acids to this medium prevents the recovery observed (*F*). Further, the addition of chloramphenicol or 6-aza uracil to the nitrogen free cultures interferes with recovery (*B*, *C*). If, however, chloramphenicol or 6-aza uracil is added after 40 min. incubation (*D*, *E*) recovery occurs. These results suggest that the recovery promoted by the M—N medium is dependent on both ribonucleic acid and protein synthesis within the first 40 min. of incubation following exposure. It is obvious that this synthesis must be minor in quantity since no nitrogen source is present in the M-N medium. It seemed plausible that the recovery promoted by the M—N medium results from the prevention, due to the nitrogen deficiency, of 'unbalanced growth'[11] during the period required for reparation of the deoxyribonucleic acid synthetic system. This hypothesis is supported by the finding that either chloramphenicol or 6-aza uridine, if added to the medium containing amino-acids (*F*) after 40 min. incubation following exposure to ultra-violet, promotes the same degree of recovery (*G*, *I*) that the M—N medium promotes (*A*). If these compounds are added immediately following exposure to ultra-violet no recovery is observed (*H*, *J*). Chloramphenicol, added immediately, prevents the recovery promoted by 6-aza uridine (*K*) and conversely the addition of 6-aza uridine immediately prevents the recovery promoted by chloramphenicol (*L*). The evidence suggests that ribonucleic acid and protein synthesis during the initial period of incubation following exposure to ultra-violet is requisite to recovery, but is detrimental to recovery afterwards. Recovery apparently requires (1) synthesis of ribonucleic acid and protein in preparation of the deoxyribonucleic acid synthetic system and (2) the prevention of inactivation through unbalanced cytoplasmic growth during the subsequent period required for resumption of synthesis of deoxyribonucleic acid.

Further details of the investigation will be published later. This project was supported in part by a contract with the U.S. Atomic Energy Commission, *AT* (40–1)–2139.

C. O. Doudney

Department of Biology,
University of Texas,
M. D. Anderson Hospital
and Tumor Institute,
Houston, Texas.
March 23.

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High Molecular Weight Ribonucleic Acids from the Nuclei of Calf Thymus

A ribonucleic acid fraction, which gives the characteristic sedimentation pattern shown in Fig. 1, has been isolated very recently from tobacco leaves[1], mouse brain[2] and microsomes of rat liver[1]. The molecular weights of components *A* and *B* are $1{\cdot}7 \times 10^6$ and $0{\cdot}6 \times 10^6$, respectively. Although the study has yet to be extended to other systems, I suggested two years ago that ribonucleic acids with molecular weights of about $1{\cdot}7 \times 10^6$ exist in the cytoplasm of many types of cells[3]. The question that naturally arises is whether ribonucleic acids of such a molecular weight also exist in a nucleus. So far no investigation along this line has been reported. The results presented below appear to provide an answer to the question.

A preparation of nuclei was obtained from calf thymus according to Allfrey and Mirsky's modification of the procedure described by Schneider and Petermann[4]. The nuclei in such a preparation have been shown to be capable of incorporating amino-acids into their proteins[4]. With the aid of Feulgen staining, the present preparation was found to contain three intact cells and sixteen cytoplasmic strands per 360 nuclei. A purified fraction of ribonucleic acids of high molecular weights was prepared from this nuclei preparation according to a procedure that will be published elsewhere[2]. The yield was 0·18 per cent

of the dry nuclei, or 13 per cent of total nucleus ribonucleic acid. (The dry nuclei contained 1·4 per cent ribonucleic acid.) As the nuclei preparation was contaminated with only 5 per cent of cytoplasm and the same procedure produces purified ribonucleic acids of high molecular weights from mouse brain at a yield of only about 20 per cent that of total brain ribonucleic acids, it is concluded that the contamination of the nucleic acid preparation from nuclei with the cytoplasmic ribonucleic acid is slight. This preparation contained less than 0·03 gm. of deoxyribonucleic acid per 100 gm. of ribonucleic acid, as estimated by diphenylamine reaction[5] and orcinal reaction[6], respectively. It had the same ultra-violet absorption spectrum as the ribonucleic acid preparation from mouse brain[7].

As indicated by the representative sedimentation diagram in Fig. 2, this preparation of nucleic acids from nuclei contained two major components (*a* and *b*) in the same ratio as that found for components *A* and *B* in whole tissue or cytoplasm (cf. Fig. 1). Moreover, the molecular weights of components *a* and *b* were found to be the same as those of components *A* and *B*, respectively.

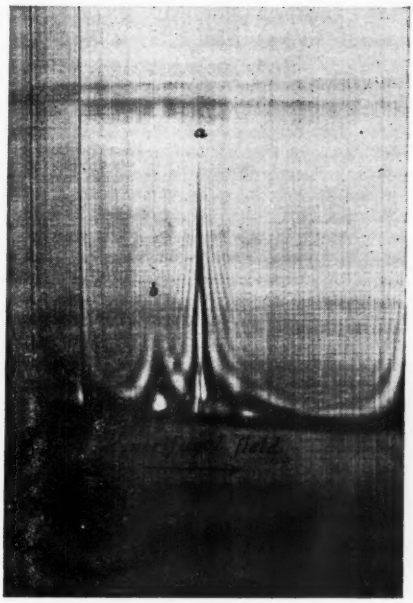

Fig. 2. Sedimentation diagram of a purified ribonucleic acid preparation from thymus nuclei. A solution of 0·25 per cent nucleic acid in 0·02 *M* phosphate, *p*H 7·3, was centrifuged in a double-sector cell at 8° C.

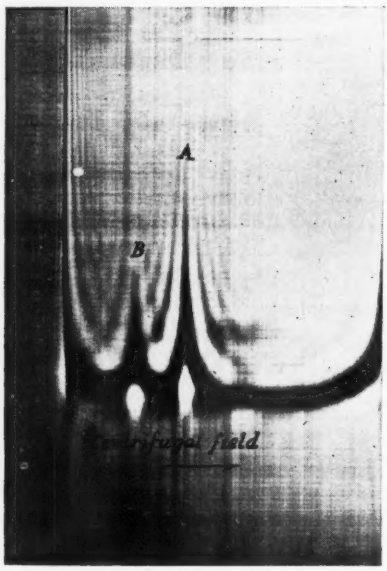

Fig. 1. Sedimentation diagram of a purified ribonucleic acid preparation from mouse brain. A solution of 0·17 per cent nucleic acid in 0·02 *M* phosphate, *p*H 7·3, was centrifuged in a single-sector cell at 8° C.

One point of difference has been observed between the ribonucleic acid preparation from whole brain and that from thymus nuclei. When a fresh preparation from the brain at a concentration of 2·5 mgm./ml. was maintained in 0·02 *M* sodium phosphate, *p*H 7·3, for 3 hr. at 3° C., it showed no detectable change in its sedimentation behaviour. If the preparation was made from brain infected with Semliki Forest virus, even its infectivity was preserved. On the other hand, when the preparation from nuclei was subjected to the same treatment, degradation occurred; single and polydisperse sedimentation boundary having a molecular weight of about $0·2 \times 10^6$ at the peak of the schlieren pattern was observed. No significant further change resulted from subsequent incubation of the preparation at a concentration of 1 mgm./ml. in 0·01 *M* phosphate for 15 min. at 83° C. This difference is tentatively attributed to the possibility that the preparation from nuclei was contaminated to a greater extent with some material possessing degrading activity than was the preparation from brain.

The presence of ribonucleic acids of high molecular weights in nuclei as well as in cytoplasms has several important implications. For example, these ribonucleic acids may be the templates for protein synthesis in both nuclei and cytoplasms.

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PING-YAO CHENG

Rockefeller Foundation Virus Laboratories,
New York, 21.
March 25.

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Post-Exposure Analysis of Organic Compounds in the Blood by a Rapid Infra-Red Technique

THERE has long been a need for a rapid standard method for the determination of levels of circulating organic compounds foreign to the blood stream. The inability to measure efficiently the blood and urine levels of compounds handled in industrial processes has hindered toxicological research and made adequate control of the working environment more difficult. The physician when establishing a diagnosis of an acute or chronic poisoning from an industrial chemical has had no ready procedure by which to identify the specific compound or to determine its concentration in the blood stream. The infra-red method to be presented satisfies the above implied criteria for an efficient analytical procedure: simplicity, rapidity, sensitivity, and availability.

10 ml. of oxalated blood are pipetted into a bacteriological culture tube with an aluminium-lined screw cap. 15 ml. of carbon bisulphide, methylene chloride, or other suitable extracting solvent is added, and the tube gently agitated by end-over-end inversion for 5 min. The tube is then centrifuged for 10 min. at 500*g*. In centrifuging carbon bisulphide mixtures a refrigerated chamber is used to minimize the explosion hazard. The solvent layer is transferred to a standard infra-red sample cell and its spectrum scanned from 2–16μ. Cells of 1 mm., 3 mm., or 16 mm. thickness are used depending on the sensitivity desired. Occasionally it is advantageous to compensate solvent absorptions by placing a matching cell with pure solvent in the reference beam of the spectrometer. While an improved optical null infra-red spectrometer[1] was used in this experiment, any standard infra-red spectrometer would have served as well.

Table 1. SOLVENT EXTRACTIONS OF BLOOD STANDARDS

Material	Concentration in blood p.p.m. (wt./vol.)	Solvent	Amount extracted p.p.m. (radioactive count)	Amount extracted p.p.m. (infra-red)
Benzene-^{14}C	74*	CS_2	68	69
			62	69
	110*	CS_2	96	88
			100	88
Trichloro-ethylene-1,2-^{14}C	25*	CS_2	28	28
			26	27
Ethanol	510†	CH_2Cl_2		135
				150
	980†	CH_2Cl_2		233
				240
*Iso*propanol	540†	CS_2		43
				40
	1,010†	CS_2		90
				83
	1,010†	CH_2Cl_2		360
				348

* By radioactive count.
† Added.

The efficiency of this method for the extraction of a given compound from blood is determined by adding a measured amount of the chemical to the blood and extracting it as outlined above. Organic compounds which are not readily soluble in the blood, such as trichloroethylene and benzene, must be checked carefully when standards are prepared, to ensure that the exact amount of chemical in solution in the blood is known before extraction. Compounds labelled with carbon-14 are employed for preparation of standards when the solubility in blood is known to be low.

This method has proved satisfactory for the measurement of many commonly employed compounds, including carbon tetrachloride, tetrachloroethylene, and 1,1,1-trichloroethane. Four organic compounds, two of which are not readily soluble in blood, are presented as examples.

Table 1 shows the results obtained upon standardization of the method while Table 2 presents the values obtained after exposure of rabbits to these chemicals.

Table 2

Rabbit	Exposure	Time after exposure (min.)	Solvent	Amount extracted p.p.m.	Calculated blood level p.p.m. (wt./vol.)*
1	Benzene, oral 2 ml./kgm.	35	CS_2	55	59
	2 ml./kgm.	75	CS_2	87	109
2	Benzene, oral 2 ml./kgm.	34	CS_2	66	71
		80	CS_2	44	47
3	Trichloroethylene-vapour 800 p.p.m. for 7 hr.	0	CS_2	9	9
		30	CS_2	2·2	2·2
4	Trichloroethylene-vapour 800 p.p.m. for 7 hr.	0	CS_2	16	16
		30	CS_2	2·5	2·5
5	Ethanol, oral 2·85 ml./kgm.	30	CH_2Cl_2	620	2,450
		60	CH_2Cl_2	728	2,900
6	Ethanol, oral 2·85 ml./kgm.	30	CH_2Cl_2	593	2,350
		60	CH_2Cl_2	675	2,700
7	*Iso*propanol, oral 2 ml./kgm.	35 (Acetone present)	CS_2	158 66	1,900
		82 (Acetone present)	CS_2	135 131	1,600
8	*Iso*propanol, oral 2 ml./kgm.	36 (Acetone present)	CS_2	159 65	1,900
		89 (Acetone present)	CS_2	115 80	1,400

* The blood levels were calculated by multiplying the amount of chemical extracted, by the efficiency of extraction determined from the values presented in Table 1.

This infra-red method for measuring post-exposure blood levels of organic compounds has many advantageous features. It is a simple, rapid procedure which can be performed in any laboratory with infra-red facilities. Although the efficiency with which different organic compounds may be extracted varies considerably, depending on both the solvent and the compound, the results indicate that the efficiency is approximately constant for any particular system. Sensitivities approaching a part per million can usually be attained by the proper choice of solvent. In addition, unknown organic compounds may be identified, more than one compound may be measured with one extraction, and metabolites, such as acetone following *iso*propanol ingestion, may be found.

The method has also been applied successfully to the analysis of urine, and should be applicable to other biological fluids as well. Work is in progress to deter-

mine more exactly the efficiency of this extraction method for the above and other organic compounds.

We wish to thank Dr. Norman Wright for suggesting this approach, and B. H. Blake for obtaining the infra-red spectra.

R. D. Stewart
D. S. Erley
T. R. Torkelson
C. L. Hake

Medical Department,
Spectroscopy Laboratory,
Biochemical Research Laboratory, of
The Dow Chemical Company, Midland, Michigan.
May 19.

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Localization of Hæmocyanin on Starch Gel Electrophoretic Patterns

Using the Smithies technique[1] of zone electrophoresis in starch gel, Woods *et al.*[2] have recently demonstrated the occurrence of several hæmocyanin proteins in the blood sera of certain crustacean species. The identification is tentatively based on the occurrence of two or more protein bands of a similar order of mobility and which are extremely concentrated in comparison to the other blood protein components.

The finding by Woods *et al.*[2] of what are assumed to be several hæmocyanins in certain species can be interpreted in the following ways: (1) as separate molecular forms of hæmocyanin, or (2) dissociation-association products or other derivatives of a single molecular form, or (3) one or more non-hæmocyanin proteins with physical properties similar to hæmocyanin but which separate from it during gel electrophoresis. Woods *et al.*[2] favour, at least in part, the second interpretation of the several constituent hæmocyanins. They further suggest that a non-copper-containing moiety may have been isolated from other components of a possible hæmocyanin polymer of higher molecular weight. In order to test the possibilities that either an intact non-hæmocyanin molecule which would not contain copper, or a hæmocyanin fragment devoid of copper may have been isolated electrophoretically, the following experiment was devised.

Crayfish serum was resolved electrophoretically in starch gel using the method of Smithies[1]. The crayfish used in this study were of two species, *Orconectes virilis* (Hagen) and *Orconectes propinquus propinquus* (Girard) (kindly identified by Prof. Horton H. Hobbs, jun. of the University of Virginia). Gels were prepared with 12·5 gm. of reagent soluble starch (Merck and Co. Ltd., Montreal, Canada)/100 ml. of borate buffer (0·02 *M* boric acid and 0·008 *M* sodium hydroxide/litre). This gave gels of *p*H 8·03. The bridge buffer used consisted of 0·20 *M* boric acid and 0·04 *M* sodium hydroxide/litre. Electrophoresis was carried out at room temperature for 12 hr. at a potential gradient of 9 v./cm. On completion of electrophoresis the gels were sectioned horizontally; one-half was stained for protein with amido-black 10*B* dye and the other half was placed for 24 hr. in a solution consisting of 50 ml. of 10 per cent aqueous sodium acetate and 3 ml. of alcoholic 0·1 per cent rubeanic acid (dithiooximide). Gomori[3] cites the development of a greenish-black colour in this reagent as a histochemical test for copper.

The two *Orconectes* species used gave patterns similar to *Cambarus limosus* (=*Orconectes limosus* (Raf.)) which had been found previously[2] to have two hæmocyanin bands. Both hæmocyanin bands of *Orconectes* stained a light greenish-black in the copper reagent. As a control the larval hæmolymph protein pattern of the eastern tent caterpillar *Malacosoma americanum* (Fab.) was subjected to the same test. *Malacosoma* has a very concentrated protein component of about the same electrophoretic mobility as the crustacean hæmocyanins. However, *Malacosoma* pattern components did not react with the reagent up to 48 hr. Serum of the horseshoe crab *Limulus polyphemus* (L.) (obtained through the courtesy of Dr. R. J. DeFalco of the Serological Museum of Rutgers University), which has an extremely concentrated fast-migrating hæmocyanin component, was also tested in this way. The concentrated component reacted positively with the copper reagent. These observations are summarized in Fig. 1.

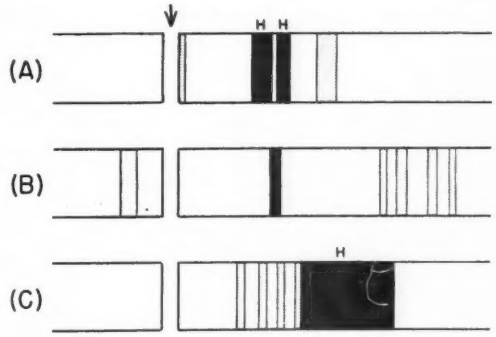

Fig. 1. Starch gel electrophoresis diagrams of the blood protein patterns of: (*A*) *Orconectes* spp., (*B*) *Malacosoma americanum* larvæ and (*C*) *Limulus polyphemus*. The anodic area is to the right of the point of sample insertion (indicated by arrow) and the cathodic area is to the left. The letter *H* indicates copper-containing components

This experiment does not support the possibility in *Orconectes* of the electrophoretic isolation of a non-hæmocyanin protein from copper-containing hæmocyanin. If there is a dissociation phenomenon involved as suggested by Woods *et al.*[2] then copper is being distributed between more than one dissociation product.

In connexion with this test yet another possibility arises. The enzyme tyrosinase also contains copper as a co-factor. This enzyme could be present as a separate electrophoretic component or absorbed to another protein. However, *M. americanum* did contain a large amount of tyrosinase in its blood as evidenced by a rapid melanization in the absence of phenylthiourea as an inhibitor. Since copper was not found to be associated with any of the *Malacosoma* protein fractions, we can probably rule out tyrosinase as a factor in these *Orconectes* experiments, where there was no appreciable darkening reaction in *Orconectes* blood.

The copper test used here provides an aid to identifying and localizing hæmocyanin on invertebrate blood protein patterns. It offers another demonstration[4,5,6] of the unique opportunities available

in using modified histochemical methods in conjunction with starch gel electrophoretic studies to give further information about the nature of particular proteins.

This work formed part of a study supported by a National Research Council of Canada grant (*T*-97) to Prof. A. S. West of Queen's University.

J. R. Whittaker*

Department of Biology,
Queen's University,
Kingston, Ontario.
June 9.

* Present address: Department of Zoology, Josiah Willard Gibbs Research Laboratory, Yale University, New Haven 11, Conn.

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PHYSIOLOGY

A Ligament in the Dorsal Aorta of Certain Fishes

Two longitudinal vertebral ligaments occur in most fishes, for example, haddock[1], one dorsal to the nerve cord in the neural arch, and one ventral to the nerve cord above the centra—though the latter is not always well developed.

Little appears to be known of a third longitudinally placed elastic fibrous ligament lying between the centra and the dorsal aorta, which is firmly attached to the basioccipitals in front, and passes to the end of the tail through the hæmal arches.

Burne in 1909 described it in the shad, *Alosa alosa* L.[2]. He suggested that it had a functional role in the movement of blood along the dorsal aorta. The ligament is virtually embedded in the dorsal aorta, projecting well into the lumen along its whole length (Fig. 1*A*) and is held straight and stationary by reason of its tautness. The whole arrangement is such that when the dorsal aorta flexes from side to side with the body movement of the living fish, the ligament "will in effect form a series of diagonal curtains passing regularly in succession down the length of the aorta. Each curtain will necessarily push the blood before it" (Burne, *loc. cit.*).

The presence of this third longitudinal ligament has been recorded in only a few fishes. No other references to it have been found save in embryological studies of the sturgeon, salmon and trout[3] and the herring[4]. No mention of it appears to be made in any textbook or laboratory manual. Its presence in the aorta of the trout was noticed by one of us (de Kock) in the course of cytological studies on fish tissues. We have since found that it is easily demonstrated in the herring (Fig. 1*B*). It shows through the wide and curiously thin-walled aorta; by bending the backbone from side to side the internal relation of ligament and blood vessel can be readily demonstrated.

If this ligament has in fact a role in the circulatory mechanism, its presence in further groups of fishes should be of considerable interest. This work is in progress and will be published in due course.

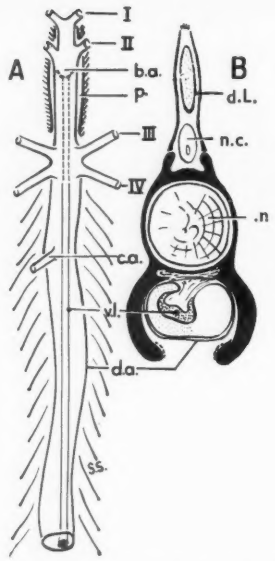

Fig. 1. *A*, Dorsal aorta of herring with ligament showing through. I–IV, Efferent branchial arteries; *b.a.*, basioccipital; *p*, bifurcation of parasphenoid; *c.a.*, cœliac artery; *v.l.*, ventral longitudinal ligament; *d.a.*, dorsal aorta; *n.c.*, nerve cord; *n.*, notochord; *d.l.*, dorsal ligament. *B*, Transverse section showing blood pushed to one side of aorta

L. L. de Kock
S. Symmons

Department of Natural History,
University of Aberdeen.
April 27.

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Formation of Polyols by the Lens of the Rat with 'Sugar' Cataract

Cataract (opacity) of the lens inevitably develops in young rats fed xylose or galactose[1], or in young diabetic rats if the blood glucose is maintained at a level above 2·5 mgm./ml. blood[2]. These three forms of cataract which resemble each other closely in clinical and histological appearance, are known as 'sugar' cataracts because in all cases there is a raised level of monosaccharides in the blood. The early metabolic changes within the lens, which lead to gradual loss of transparency, are unknown. It was decided to examine the carbohydrates and their derivatives in normal and cataractous lenses to see if changes occurred in 'sugar' cataract, and if so whether there was any similarity in this respect between the three forms of cataract.

Cataract was induced in young rats (3 weeks old) by feeding a diet[3] containing 35 per cent xylose or 35 per cent galactose and in older rats (4–8 weeks old) by rendering them diabetic with subcutaneous injections of alloxan[4]. The rats were usually killed when the first signs of cataract were visible clinically and trichloroacetic acid extracts of the lenses were made and compared with those from rats fed a diet containing 35 per cent glucose or on the standard diet (pellets, Oxo, Ltd.).

The acid extracts of lens were concentrated and examined by paper chromatography and paper electrophoresis[5]. The lens of the young rat fed 35 per cent glucose, or pellets, contained inositol (0·2–0·5 mgm./gm. lens) and glucose (0·1–0·2 mgm./gm. lens). There were no other carbohydrates at a comparable concentration.

In the lens made cataractous in all three ways inositol was present at a concentration similar to that in normal lens. Table 1 summarizes the findings with respect to the other carbohydrate derivatives found in the cataractous lens. The lens of the rat fed with xylose contained a high concentration of xylitol, and a lower concentration of sorbitol. Traces of glucose and xylose were occasionally present. The lens of the rat fed with galactose contained dulcitol (galactitol), and sometimes a trace of galactose. The lens of the alloxan-diabetic rat contained sorbitol and a lower concentration of glucose and/or fructose (0·5 mgm./gm. lens).

The polyols were present in the lens of the xylose and galactose-fed rats after 1–2 days on the diet, before cataract was visible. Xylose cataract is not permanent and regresses even when the diet is continued; the lens even after recovery was found to contain a high level of xylitol[5]. Sorbitol was found at a concentration of 0·5 and 2·0 mgm./gm. lens in the lenses of two rats which died after being diabetic for 5 days; but the lenses from five alloxan-treated rats the blood sugar-level of which had fallen from above 2·5 mgm./ml. to a normal level contained only traces of sorbitol.

Table 1

Diet or treatment	Concentration of polyols in lens in early stages of cataract (mgm./gm.)		
	Sorbitol	Xylitol	Dulcitol
35 per cent glucose	—	—	—
35 per cent xylose	0·4	4·0	—
35 per cent galactose	—	—	20·0
Pellets (normal rats)	trace	—	—
Pellets (alloxandiabetic rats)	4·0	—	—

Dialysed extracts of rat lens were found to reduce the aldo-sugars xylose, galactose and glucose, in the presence of reduced triphosphopyridine nucleotide and this presumably is the route by which the polyol is formed *in vivo*. The polyols, xylitol, dulcitol and sorbitol, were oxidized by lens extracts in the presence of triphosphopyridine nucleotide; in the case of xylitol the oxidation product was identified as xylose[5]. Apart from the lens, the placenta and seminal vesicles are the only animal tissues known to contain an enzyme which reduces aldoses using triphosphopyridine nucleotide as coenzyme[6]. Extracts of rat lens will also oxidize xylitol and sorbitol in the presence of diphosphopyridine nucleotide to the corresponding keto sugars, xylulose and fructose[7].

The blood, liver, spleen, lung, kidney, heart and leg muscles of the weanling rat fed with xylose and galactose were examined for polyols. None were detected in the organs of the xylose-fed rat. The heart and leg muscle of the galactose-fed rat contained dulcitol, though at a lower concentration than in the lens.

In man xylose cataract is unknown. Galactose cataract is the result of a rare inborn error of metabolism in which an infant becomes galactosæmic as a result of its inability to metabolize galactose. Diabetic cataract is a rare complication of juvenile diabetes. It is a debatable point whether cataract in older diabetics differs from other forms of senile cataract. Five senile cataracts from non-diabetic patients and two from diabetic patients were examined. Only the two lenses from the diabetic patients were found to contain sorbitol.

It is not possible to say whether the accumulation of polyols in the lens is the cause of the cataract. Xylose and galactose are not normally encountered by the lens; but glucose is its main nutrient. Since the mechanism for its reduction to sorbitol is present in normal lens it seems likely that its formation is a normal metabolic occurrence, but the path by which it is broken down is blocked in diabetes.

Ruth van Heyningen

Nuffield Laboratory of Ophthalmology,
University of Oxford.
June 13.

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Changes in Fluorescence in a Frog Sartorius Muscle Following a Twitch

In a recent publication[1] it was proposed that the blue autofluorescence of living tissues may largely be due to the reduced pyridine nucleotide of the mitochondria. An opportunity to test this hypothesis is afforded by the specific response of the intramitochondrial pyridine nucleotide to an increase of concentration of adenosine diphosphate following a muscle twitch. This increase of concentration of adenosine diphosphate has been shown by spectrophotometric observations to cause an oxidation of reduced pyridine nucleotide of the mitochondria both in the isolated mitochondria[2] and intact muscles[3]. Thus muscle contraction elicits a specific response of intramitochondrial pyridine nucleotide. Such a specific test is required to distinguish between the fluorescence of cytoplasmic and mitochondrial pyridine nucleotides because both may be bound forms and therefore have indistinguishable maxima at 443 mμ [4].

We have carried out a sensitive measurement of the kinetics of changes in the autofluorescence of frog sartorious muscle following a twitch with two purposes in mind: (1) To provide support for the idea that the autofluorescence of the living tissue is due to intramitochondrial reduced pyridine nucleotide and (2) to demonstrate the use of the fluorescence method for following adenosine diphosphate changes in the muscle following a twitch as a supplement to the spectrophotometric method.

The design of the fluorescence apparatus is similar to that of Theorell[5]. This apparatus has been thoroughly tested for its response to reduced pyridine nucleotide of mitochondrial suspensions[6]. It consists of a 100-watt mercury arc lamp illuminating the muscle strip through a 366 mμ filter ('Eppendorf'). A portion of the light is reflected on to a photocell for controlling the intensity of the arc by means of a feedback circuit. The exciting light falls upon the muscle obliquely and the emitted light is measured by a type 6342 electron multiplier photocell placed as

close as possible to the muscle. The photocell is protected from the 366 mμ radiation by a Wratten *W*-2 filter or by a combination of this filter with a Bausch and Lomb interference filter transmitting a 15 mμ band peaking at 450 mμ. Both filter combinations gave satisfactory results. The photocurrent was amplified by high gain chopper amplifiers and recorded by a galvanometer oscillograph. A 'bucking-out' circuit was used and the increment of fluorescence caused by electrical stimulation is recorded. The scale of the ordinate is given by independent spectrophotometric measurements (Fig. 1).

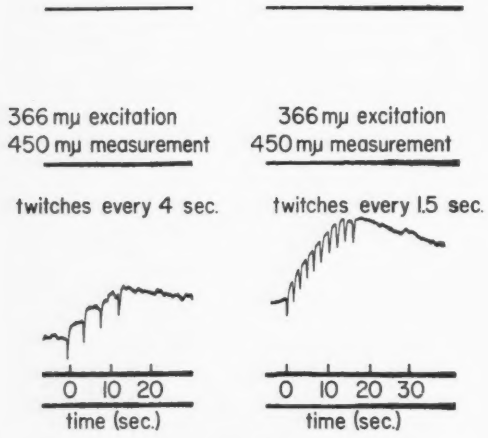

Fig. 1. Fluorescence response of frog sartorious muscle to electrical contraction at 4 (left) and 1·5 (right) second intervals. The right-hand record indicates a 'saturating' effect. Independent spectrophotometric studies give the concentration scale for the ordinate: this saturating effect corresponds to the oxidation of 0·035 μmoles/gm. reduced pyridine nucleotide (ref. 8)

The excised frog's sartorious muscle was contained in a holder where oxygenated Ringer flowed freely past the exposed portion of the muscle[3,7]. The muscle and the bathing fluid were cooled to 8°.

Fig. 1 illustrates two responses of the fluorescence of the sartorious muscle to a series of twitches. Electrical stimulation is applied every 4 sec. in one case and every 1·5 sec. in the other case. The twitch of the muscle is indicated as the small and abrupt deflexion on the trace which marks the moment of contraction. There is a decrease of fluorescence in a staircase fashion for the lower stimulation rate. At the higher stimulation rate the fluorescence change reaches a plateau, beyond which further stimulation causes little change. A comparison of these results with those obtained spectrophotometrically[3] suggests that the same phenomenon is being recorded in both cases: the oxidation of reduced pyridine nucleotide caused by increased adenosine diphosphate concentration at the mitochondria. It we then accept the similarities of the kinetics as sufficient basis to identify the fluorescence decreases changes with the oxidation of intramitochondrial reduced pyridine nucleotide, we can make the following statement. (1) The concentration of adenosine diphosphate arriving at the mitochondria following a single twitch is a small fraction of that required for half-maximal activation of spectroscopic effects in isolated mitochondria (0·056 μmoles/gm.[2,3]). (2) The staircase response for the 4 sec. twitches emphasizes that the low concentration of adenosine diphosphate per twitch applies not only to the first twitch but also the second and possibly later twitches of the frog sartorious muscle.

This method has much to recommend it in terms of simplicity and sensitivity. In addition it may have the further advantages of (*a*) being applicable to a thick layer of muscle and (*b*) being relatively insensitive to hæmoglobin. It may therefore be much more readily applicable to intact tissues than the spectrophotometric method.

Britton Chance
Frans Jöbsis

Johnson Research Foundation,
University of Pennsylvania.

May 24.

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Frequencies of the Haptoglobin Groups in 406 French Blood Donors

The method of zone electrophoresis in starch gel enabled Smithies[1] to describe three haptoglobin groups in human sera. Using a standard technique previously reported[2,3] we have examined the sera of 406 blood donors living in Paris. In each 'Plexiglas' tray (internal dimensions 234 mm. × 80 mm. × 6 mm.) three serum samples mixed with a hæmoglobin solution (0·05 ml. of a solution containing 50 mgm. of hæmoglobin being added to 1 ml. of serum) were allowed to migrate simultaneously, side by side, for 18 hr., under a potential of 100 V. After electrophoresis the starch gels were divided into two slices and stained, one with amido black, and the other with benzidine reagent for peroxidase activity. The technique was the same as that previously described and used to detect hæmoglobins in agar gels[4] but without using zinc acetate as a solution.

The haptoglobin groups were quite easily identified (Figs. 1 and 2). Particularly the difference between Hp 1–2 and Hp 2–2 was clear-cut: their electrophoretic patterns are very different and it will be seen that the haptoglobin–hæmoglobin complex moves more slowly in group 2–2 than in group 1–2.

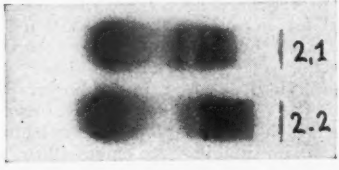

Fig. 1

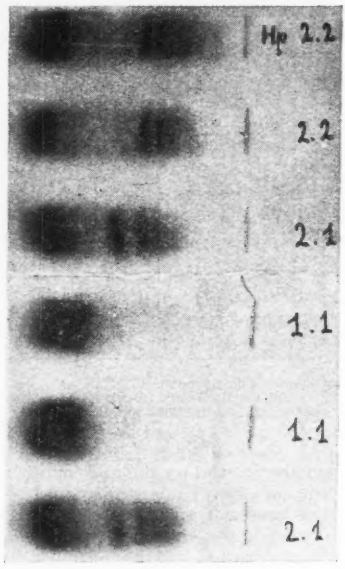

Fig. 2

The frequencies of the three groups are in agreement ($\chi^2 = 0{\cdot}505$, for 1 degree of freedom) with the genetical theory proposed by Smithies and Ford Walker[5] (Table 1). The gene frequencies are : $Hp^1 = 0{\cdot}4015$, and $Hp^2 = 0{\cdot}5985$. These figures are not significantly different from those already reported, in populations of European origin by some workers, particularly from the important series of Galatius-Jensen in Denmark. No mention is made in Table 1 of the results collected in a British and in a Basque sample by Allison *et al.*[6], who found a fourth haptoglobin group (0–0) and whose British series differs significantly from the expected frequencies calculated from the simple two-alleles theory. We shall not discuss the interesting finding of the 0–0 group not the cause of the discrepancy : presumably it is attributable to differences in technique.

Table 1

Authors	Total (*N*)	Haptoglobin groups					
		1 – 1		1 – 2		2 – 2	
		No.	Percentage	No.	Percentage	No.	Percentage
Sutton *et al.* (ref. 7) (U.S.A., Canada*)	103	16	15·53	54	52·43	33	32·04
Galatius-Jensen (ref. 8) (Denmark)	2,046	328	16·03	967	47·26	751	36·71
Laurell and Grubb (ref. 9) (Sweden)	46		15†		50†		35†
Fleischer and Lundevall (ref. 10) (Norway)	500		16†		45†		38†
Present survey (France)	406	62	15·27	202	49·75	142	34·98

* Quoted from Sutton *et al.* who pooled the figures given by Smithies with their own.
† The percentage only was given in the original paper.

If we use only comparable figures, it seems reasonable to consider, from the results of Sutton *et al.*, Smithies, Galatius-Jensen, Laurell and Grubb, Fleischer and Lundevall, and from our own results, that in most of the populations living in the occidental and septentrional part of Europe and in the white population of America, the frequencies of the genes Hp^1 and Hp^2 do not differ appreciably from 40 to 60 per cent respectively. We agree, however, that the complete system may be much more complicated.

J. Moullec
J. M. Fine

Centre National de Transfusion Sanguine,
Paris.
March 25.

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RADIO BIOLOGY

Increased Oxygen Consumption in Rats during Irradiation

Metabolic changes arising during irradiation are of great importance for understanding the mechanism of the effects of radiation. In work on such changes in rats we have used the estimation of oxygen consumption as a general indicator of the metabolic state.

We used 40 rats (Wistar strain), females, average weight 190 gm. ; oxygen consumption was measured during irradiation at a dose-rate of 50 r./min. in every animal separately. The measurements were carried out in boxes 8 cm. × 8 cm. × 16 cm. The amount of air passing the box was regulated in accordance with the body-weight of the experimental animal, and was determined by the following formula : Amount of air ($cm.^3/in.^{-1}$) = weight of animal (g) × 2·5. The procedure was as follows. The animals were kept in the box for 50 min. During the first 20 min. they became adapted to the experimental conditions. In the period 20–50 min. oxygen consumption was measured. The oxygen consumption between the 20th and 30th minute was taken as the basic value (100 per cent). During the period 30–50 min. the rats were subjected to total-body irradiation (180 kV., 15 m.amp., 1 aluminium, 0·5 copper, focal distance 40 cm., dose-rate 50 r./min.).

The oxygen consumption of control animals was measured under the same conditions but without irradiation, and they were exposed to the noise caused by opening the lead diaphragm of the X-ray tube. This noise had no influence on the oxygen consumption of control animals.

The comparison of oxygen consumption of experimental and control animals is given in Fig. 1.

At the time of decreasing oxygen consumption in control rats, that of irradiated rats rises. Increased consumption of oxygen takes place during the first

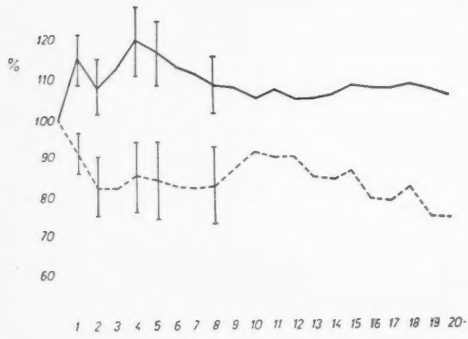

Fig. 1. Comparison of the changes in oxygen consumption of control (– – –) and irradiated (——) rats. Standard error level is given by vertical lines

minute (50 r.), at the fourth minute it reaches the maximum (200 r.) and in the tenth minute it approaches the values before irradiation, but is still higher than in control animals.

The difference in oxygen consumption in twenty irradiated and twenty control animals during the period from the first to the eighth minute of irradiation is statistically significant ($P > 0.01$).

We have found in the literature two reports on changes in respiratory metabolism during irradiation. In both cases the oxygen consumption was increased at higher doses of radiation than those we have used. In the first case, the rate of oxygen consumption was raised after a dose of 1,000 r. in monkeys. In the second case, oxygen consumption of rats and mice was increased during irradiation with a dose-rate of 100 r./min. Our results are in accord with these; significant changes were found after the relatively low dose of 50 r.

A. Vacek

Biophysical Institute,
Academy of Sciences,
Brno, Czechoslovakia.

April 18.

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Prophylactic Effects of Amine Oxides in Radiation Injury in Mice

In 1957, Haley *et al.*[1] found that quinoxaline-1,4-di-N-oxide reduced X-radiation mortality in mice by 50 per cent. Two mechanisms were involved, reduction of bacteræmia[1] and interaction with X-ray-produced oxidizing radicals[2]. Comparisons have been made of other N-oxides (Table 1) using groups of 20 *CF*-1 mice and the same radiation conditions as before[1]. The 250 mgm./kgm. oral dose of drugs was given 24 hr. prior to irradiation with 550 r. The two quinoxaline derivatives significantly increased the ST_{50} day but had less effect on total survival than quinoxaline-1,4-di-N-oxide. Erythromycin N-oxide significantly reduced the ST_{50} day and total survival while its anhydro derivative was equivalent to quinoxaline-1,4-di-N-oxide as a radiation prophylactic. All the above compounds are readily absorbed, excreted slowly in the urine and exert antibiotic effects so the radiation bacteræmia could be reduced. On the other hand not all of them can interact with equal facility with the radiation-produced oxidizing radicals. Examination of the chemical structures involved indicated that an amine oxide either in an unsaturated ring, for example, quinoxaline or within one carbon atom of a double bond, for example, anhydroerythromycin is necessary if oxidizing radicals are to be prevented from exerting their deleterious effects. In the dimethyl-substituted quinoxaline compounds difficulties in oxidizing the methyl groups are probably the reason for the decrease in protectant activity even though Francis *et al.*[4] showed that hydroxylation in the 2 position occurs *in vivo*. With erythromycin N-oxide, the double bond is lacking and the compound can be oxidized only with difficulty even *in vitro*[5]. Thus, it would appear that amine oxides with the above chemical structures can reduce mortality from ionizing radiation when administered orally 24 hr. prior to exposure.

Table 1. Orally Administered Amine Oxides and Survival after X-Irradiation

Treatment	ST_{50}* and range Days	Slope and range	Total mortality Per cent	Day
Saline control	9·4 (8·4–10·5)	1·29 (1·19–1·40)	100	14
2 : 3-Dimethyl-quinoxaline-1,4-di-N-oxide	12·4 (10·1–15·2)	1·56 (1·32–1·84)	85	30
6-Chloro-2 : 3-dimethyl quinoxaline-1,4-di-N-oxide	13·4 (10·9–16·6)	1·60 (1·35–1·90)	80	30
Saline control	12·3 (10·6–14·3)	1·41 (1·26–1·59)	90	30
Erythromycin N-oxide	10·0 (9·0–11·2)	1·29 (1·19–1·40)	100	18
Anhydroerythromycin N-oxide	—	—	45	30

* ST_{50}, day upon which 50 per cent of animals are expected to be still alive. Confidence limits are calculated at $P = 0.05$ (ref. 3). All drugs 250 mgm./kgm. orally 24 hr. pre-irradiation.

We wish to thank Imperial Chemical Industries, Ltd., for the quinoxaline compounds and Lilly Research Laboratories for the erythromycin compounds. This work is based on work performed under Contract No. *AT* (04-1)–*GEN*-12 between the Atomic Energy Commission and the University of California at Los Angeles.

Thomas J. Haley
Anna M. Flesher
Nathan Komesu

Department and Laboratories of
Nuclear Medicine and Radiation Biology,
School of Medicine,
University of California,
Los Angeles.

May 22.

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PATHOLOGY

Formation of the Toxoid of Histamine Sensitizing Factor in *Bordetella pertussis*

It has been reported that mice injected with *Bordetella pertussis* vaccine become exceedingly sensitive to histamine[1]. Maitland *et al.*[2] found that antibacterial rabbit sera against *Bordetella pertussis* contain antibodies to histamine sensitizing factor. However, it seems that no biological definition of histamine sensitizing factor has been established. We believe that it is a toxin different from the accepted *pertussis* toxin. The present communication deals with formation of the toxoid of histamine sensitizing factor in *Bordetella pertussis* with the use of formalin.

The supernatant of a culture of *Bordetella pertussis*, strain 18–323, was prepared by a method already described[3]. Formalin was added to the supernatant to give a concentration of 0·5 per cent. After various intervals of incubation at 37° C., the degrees of detoxification of the histamine sensitizing factor were examined. Tests of the antigenicity of the toxoid thus formed were also carried out.

0·5 ml. of culture supernatant to which formalin had been added was injected intraperitoneally into *dd* mice, weighing about 20 gm. each. Five days later the sensitivity to histamine of an inoculated group of mice was tested to determine the degree of detoxification. The mice surviving the histamine-sensitivity test were inoculated 14 days later with either *pertussis* vaccine or culture supernatant in order to determine whether they were immune. Five days later their sensitivity to histamine was retested. (Table 1).

Table 1. Detoxification of Histamine Sensitizing Factor in Culture Supernatant and Active Immunization of Mice with Toxoid of Histamine Sensitizing Factor

Incubation period of formalized culture supernatant at 37° C.	Detoxification (loss of histamine sensitizing ability)	Immunization with toxoid against histamine sensitizing factor
4 days	incomplete	no immunity
7 days	complete	complete immunity
10 days	complete	no immunity
15 days	complete	no immunity
Control: Culture supernatant heated at 56° C. for 30 min.	no detoxification	no immunity

As shown in Table 1, the culture supernatant heated at 56° C. and containing histamine sensitizing factor without *pertussis* exotoxic activity, afforded the mice no immunity against histamine sensitizing factor. The antigen, when detoxified incompletely or incubated for a prolonged period (perhaps due to partial denaturation) gave the mice no immunity against histamine sensitizing factor; whereas a single injection of complete toxoid established complete immunity against it. Repeated administrations of an incompletely detoxified antigen gave no immunity. However, repeated injections of antigen after prolonged incubation afforded partial immunological protection. These findings suggest that even the presence of a small fraction of histamine sensitizing factor in *pertussis* antigens interferes with the establishment of immunity against it. The incubation period required for the formation of the complete toxoid is subject to variation according to the preparation used.

The incubation period necessary for formation of toxoid of vaccine, in general, seems shorter than that of culture supernatant. It was estimated to be about 24 hr. at 37° C. Formation of the toxoid did not occur following the addition of phenol or merthiolate to the antigen. The heating of the antigen at 80° C. for 30 min. resulted in complete inactivation of histamine sensitizing factor and destruction of the antigenicity.

24 hr. after intraperitoneal injection of 0·5 ml. of freshly isolated sera of rabbit immunized with the toxoid, the mice received intraperitoneal injections of 0·5 ml.(15×10^{10} organisms) of *pertussis* vaccine (killed by heating at 56° C.) to test for the possible production of antibodies against histamine sensitizing factor. Five days later histamine sensitization was examined. One *LD*50 for a control group without immune serum was 29·8 mgm./kgm. of histamine, while the *LD*50 for one group of passively immunized mice was more than 480 mgm./kgm., affording good evidence for the presence of antibodies against histamine sensitizing factor.

Rabbit immune sera were able to prevent a reduction in histamine inactivation of a homogenate of the organs of *pertussis*-sensitized mice[4], when the sera were inoculated 24 hr. before administration of *pertussis* vaccine.

Thus, it seems reasonable to regard histamine sensitizing factor as a toxin, which apparently has nothing to do with preventive antigen(s)[5].

Immunologically it was demonstrated on rabbit sera immune against the toxoid of histamine sensitizing factor that the histamine sensitization due to *pertussis* vaccine has nothing to do with anaphylactic shock against horse serum.

Maitland *et al.*[2] and Stronk and Pittman[6] reported that guinea pigs show no increase in susceptibility after the administration of *pertussis* vaccine. Nevertheless, we found a marked reduction in histaminase activity of a homogenate of organs from *pertussis*-sensitized guinea pigs using Kapeller-Adler's method[7]. No reduction was observed in the histamine inactivation of a homogenate where guinea pig ileum was employed following an extraction of histamine by a modified version of McIntire's method[8]. However, at an early stage (first 2–3 hr.) of the reaction between the homogenate and histamine, a marked reduction in histamine inactivation was observed when guinea pig ileum was used. The explanation of histamine sensitization in mice and rats, must await further studies, although a reduced activity in histaminase or histamine inactivation may account for a large part of the sensitization to histamine.

For the production of *pertussis* vaccine the existence of histamine sensitizing factor in *pertussis* antigens should not be neglected, because evidence for the existence of antibodies against histamine sensitizing factor in a human hyper-immune serum was recently reported by Maitland and Guerault[9].

Toshitaka Matsui
Yoshio Kuwajima

Department of Bacteriology,
Osaka City University Medical School,
Osaka.

March 14.

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Effect of Chlorpromazine on Crocker Sarcoma and Ehrlich Ascites Carcinoma

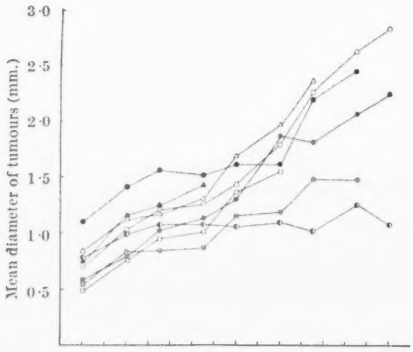
Goldin *et al.*[1] and Humpreys *et al.*[2] have stated that reserpine treatment in mice bearing transplanted leukæmia *L* 1210 caused regression of neoplasm and prolonged the survival time of these animals. These observations have directed attention to other tranquillizers as possible anticarcinogenic drugs. The growth of sarcoma 37 was inhibited by chlorpromazine treatment[3]. However, according to Cranston[4] some tranquillizers belonging to the phenothiazine group did not show any inhibitory effects on mammary adenocarcinomas in mice.

In our Department we have carried out some experiments dealing with the effects of chlorpromazine on Crocker sarcoma and Ehrlich ascites carcinoma in mice.

R III, B_N (an inbred strain from our own animal colony) and Swiss mice of both sexes were used. The initial weight of mice was 25–30 gm. Chlorpromazine ('Largactil'—Société Parisienne d'Expansion Chimique S.A., Specia) was given daily intraperitoneally at a dose of 2·5 mgm./kgm. body-weight in about 0·25 ml. physiological saline. A control group was given saline alone.

The rate of growth of Crocker sarcomas was measured by the mean diameter of the tumours, and that of Ehrlich ascites carcinomas by daily weighings of the mice and by noting their survival times.

The growth of Crocker sarcomas in chlorpromazine-treated and control mice is shown in Fig. 1. Chlorpromazine seems to have no inhibitory effect on this neoplasm—the tumours grew at the same rate as in the control group, despite the depressive effect of chlorpromazine on mice.



(*a*)

Chlorpromazine did not prolong the survival time in *R* III mice bearing Ehrlich ascites carcinoma (Table 1). However, the gain in weight of these mice was much smaller than that in control mice. The diminished gain in weight was due to the smaller gain in carcass weight, as well as to smaller production of ascites fluid. Analogous results were obtained with Swiss mice (Table 1).

Thus chlorpromazine had no inhibitory effect on the growth of either tumour despite the depressive

Table 1. Survival Time and Weight Changes of *R* III and Swiss Mice bearing Ehrlich Ascites Carcinoma

Strain and sex	Group	Days after transplantation																
		1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17
R III ♂	Control																	
	No. of surviving animals	14	14	14	14	13	13	13	13	13	13	13	12	11	11	8	5	2
	Average weight gain/mouse (gm.)	0·0	−0·5	−0·2	−0·1	2·0	1·3	2·4	4·1	4·6	4·8	5·5	5·2	3·8	4·1	3·8	5·1	7·8
R III ♂	Chlorpromazine†																	
	No. of surviving animals	14	14	14	14	14	14	14	14	14	14	14	14	14	4	3	—	—
	Average weight gain/mouse (gm.)*	0·0	−0·7	−0·4	3·3	0·9	1·8	2·2	2·2	3·2	2·0	1·1	0·8	3·0	−2·2	−1·0	—	—
R III ♂	Chlorpromazine‡																	
	No. of surviving animals	5	5	5	5	5	5	5	5	5	5	3	3	2	—	—	—	—
	Average weight gain/mouse (gm.)*	0·0	−0·1	−0·3	0·4	0·7	0·9	0·9	0·7	0·5	0·3	1·4	0·6	0·2	—	—	—	—
Swiss ♂	Control																	
	No. of surviving animals	15	15	15	15	15	15	15	15	15	15	15	14	12	6	1	—	—
	Average weight gain/mouse (gm.)*	0·0	1·2	−0·4	−1·0	−0·4	1·4	2·1	3·6	5·0	5·5	5·1	5·0	4·0	5·0	5·6	—	—
Swiss ♂	Chlorpromazine†																	
	No. of surviving animals	15	15	15	15	15	15	15	15	15	15	11	11	9	4	1	—	—
	Average weight gain/mouse (gm.)*	0·0	1·0	0·2	−0·7	−0·5	1·2	0·8	1·1	1·1	1·1	3·3	2·2	3·6	8·0	2·2	—	—

* Weight changes as compared to the weight on the first day after tumour implantation.
† 2·5 mgm./kgm. body-weight every day until twelfth day after implantation of tumours.
‡ 2·5 mgm./kgm. body-weight every two days.
The treatment was started on the first day after tumour transplantation.

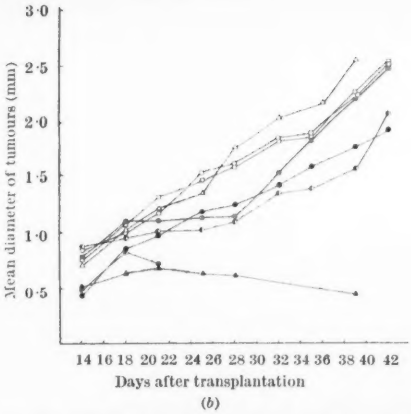


Fig. 1. The growth of Crocker sarcoma in *BN* mice. The rate of tumour growth is expressed as a mean diameter of the tumour (arithmetical mean of three diameters at right angles). Each curve represents the growth of single tumour. (*a*) Control mice; (*b*) chlorpromazine-treated mice

action of the drug. The daily dose administered by us was much smaller than that given by Belkin and Hardy[3]. We found that a single dose of 10 mgm./kgm., that is, five times smaller than that used by Belkin and Hardy, caused a high mortality among the animals.

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M. Chorazy

Department of Tumour Biology,
Institute of Oncology,
Gliwice, Poland.
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Inhibition of Tumour Growth with 2:5-Dicarbethoxy-3:4-Dihydroxy-Thiophene

The possibility of preferential inhibition of tumour growth with antimetabolites of hexose monophosphate pathway intermediates was suggested by Sahasrabudhe[1]. In pursuance of this suggestion it was shown that thiophene-2 : 5-dicarboxylic acid, administered as its sodium salt, significantly inhibited the growth of transplantable fibrosarcoma in mice, and also increased the survival of Yoshida (ascites) sarcoma-bearing rats[2]. It was further shown that since this sodium salt is soluble in water, it was probably excreted rapidly. When the total daily dose of thiophene-2 : 5-dicarboxylic acid was increased and the injection schedule evenly spaced during the day to maintain adequate drug concentration, it was found that the inhibitory effects were significantly enhanced. It was therefore felt that if the free carboxy groups of the acid were esterified to reduce its solubility in water, the drug concentration might remain steady in the system for longer periods. In addition to this, if two hydroxy groups are introduced at the third and fourth positions of the thiophene-2 : 5-dicarboxylic acid molecule, it was thought that the resemblance between the sugar intermediates of the hexose monophosphate pathway and the antimetabolite would be increased, and the effectivity against cancer might also increase. With these objectives in view 2 : 5-dicarbethoxy-3 : 4-dihydroxy-thiophene (hereafter referred as 'Dicetol') was synthesized[3]. Dicetol is insoluble in water and therefore it was converted into a water-soluble disodio-dicetol by treatment with ethanolic sodium ethoxide, to facilitate its administration in aqueous medium. Disodio-dicetol readily hydrolyses in the presence of carbon dioxide. It was therefore felt that the water-soluble compound, used for practical reasons, would be transformed in the body into an insoluble dicetol, which would probably be retained in the system for longer periods. The present communication reports the results of preliminary screening trials with disodio-dicetol.

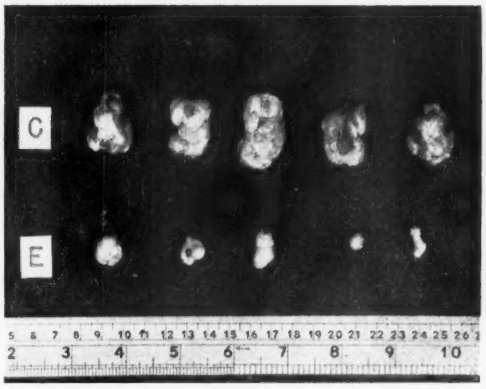

Fig. 1. Inhibition of growth of transplantable fibrosarcoma with disodio-dicetol. Top row (*C*) tumours from control group. Weight of tumours in this group are, from left to right, 4·14, 3·61, 5·47, 4·56 and 4·33 gm. respectively. Bottom row (*E*) shows tumours from treated group. Weights of tumours in treated group, from left to right, are 1·12, 0·49, 0·92, 0·19 and 0·12 gm. respectively. Treatment was started on the eighth day after transplantation and continued for 15 days. Dose 150 mgm./kgm. body-weight/day of disodio-dicetol

Six- to eight-weeks-old Swiss mice weighing 20–25 gm. were used. The transplantable fibrosarcoma used in the present investigation was originally obtained by Waravdekar and Ranadive[4] from animals treated with 6 : 12-dimethylbenzo-(1 : 2-*b*, 4 : 5-*b'*)-dithionaphthalene. This has since been maintained in Swiss mice through several serial transplantations. Freshly dissected tumours were chopped to fine pieces and a homogeneous suspension made in normal saline. 0·5 ml. of the tumour suspension was injected subcutaneously in each of the animals and the tumours allowed to grow for 8 days. Animals having uniform tumour sizes (visual observation) were divided into two groups. In the experimental group each of the animals received subcutaneous injections of disodio-dicetol in normal saline (1 mgm./0·5 ml.) at 0900, 1500 and 2100 hr. every day (total daily dose 3 mgm./animal). The corresponding control group received 0·5 ml. normal saline only at the times mentioned. Injections were continued for 15 days. The animals were then killed and the weights and dimensions of the tumours determined. Fig. 1 shows the tumours from the control and treated groups placed side by side. The weights of individual tumours are indicated in the legend. The weights of tumours from the control group varied from 3·6 to

5·4 gm., whereas those from the treated group ranged from 0·12 to 1·12 gm. Thus there was significant inhibition of tumour growth in treated animals. Apart from the general reduction in the weights of the tumours in the treated group, there was evidence of regression in tumour size in some animals as can be seen from *E*4 and *E*5 in Fig. 1. Further, it is of interest to note that with the doses employed in the present investigation (3 mgm./day/animal, that is, 150 mgm./kgm. body-weight/day for 15 days) there were no apparent signs of toxicity in the treated animals. Further work is in progress, details of which will be reported elsewhere.

M. B. Sahasrabudhe
M. V. Narurkar
L. B. Kotnis
Biology Division,
Atomic Energy Establishment Trombay,
Indian Cancer Research Centre,
Parel, Bombay 12.
B. D. Tilak
M. D. Bhavsar
University Department of Chemical Technology,
Matunga, Bombay.
March 31.

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Appearance of Granules in the Cytoplasm of Tumour-Cell Cultures in Contact with Lysozyme

We have tried to establish whether or not lysozyme added in appropriate concentrations to human tumour cell cultures can produce some morphological changes in such cells. The following human tumour cells were utilized: strain *Af* (H.Ep 2) of epithelial nature and strain *A* (H.S. 1) of mesenchymal origin. These strains were kindly supplied by Dr. A. Fjelde, State Serum Institute, Copenhagen.

Gey's liquid medium, without addition of antibiotics, was used in roller tubes. The colonies were treated two or four days after culturing and after growth had been found to be normal. At this point the liquid medium in the tube was replaced by another containing lysozyme chloride in the following dilutions: 0·1, 1, 2·5, and 5 mgm./ml. medium. The control tubes contained normal Gey's medium, without lysozyme.

The tumour colonies were tested after 20-min., 1-hr., 5-hr., 10-hr., 24-hr., 48-hr. and 6-days contact with the medium containing lysozyme. Slides for microscopic examination were prepared from these cells. Smears were made by using a thin rectangular strip of blotting paper, the cell colony being made to adhere to one end; the blotting paper was then gently passed over the slide, so producing a smear. After drying, the smears were fixed and stained with May-Grünwald's and Giemsa's stains.

Many azurophil granules of various sizes (approximately 1 mμ diam.) were observed in the protoplasm of numerous cells from the *Af* (carcinoma) and *A* (sarcoma) colonies treated with 2·5 and 5 mgm./ml. of lysozome chloride. These granules became evident, even if small and not very clearly distinguishable, after 20-min. contact with lysozyme, becoming more obvious and reaching the largest size after 48 hr. or more.

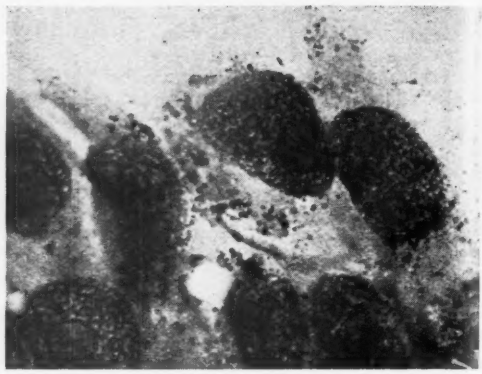

Fig. 1. Photomicrograph of human cancer cell (*Af*) treated with lysozyme: the cytoplasma granules are visible. (× 300)

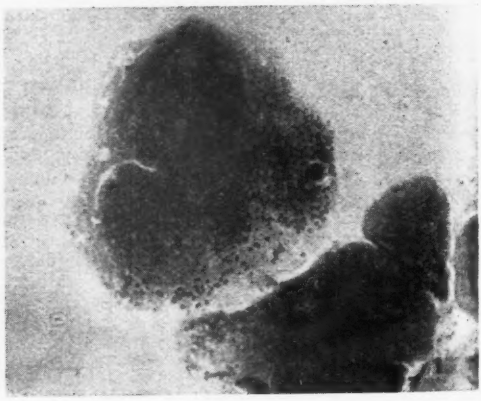

Fig. 2. Photomicrograph of human sarcoma cells (*A*) treated with lysozyme: the cytoplasma granules are visible. (× 300)

The Hela strain cultivated in Hanks medium, in stationary cultures, gave the same results. The above-mentioned type of granular formations were not observed in the controls.

Other tests were performed on fibroblasts from chick embryos, human kidney cells and monkey kidney cells cultivated both in Gey's and Hanks medium and in roller or stationary tubes. Granules did not appear in the fibroblasts, but were, in contrast, seen in human and monkey kidney cells. However, they appeared much later (after 24 hr.) than in tumour cells, and their number was much lower.

Another test was performed on cells taken from the ascitic fluid of a patient with cancer of the peritoneum. The cells were seeded in Gey's medium, following the roller tube method, and the lysozyme added immediately. The granules were very numerous in the tumour cells but absent from the cytoplasm of the lymphocytic type cells present in the liquid.

The following tests were performed in order to determine the chemical nature of the granules:

(1) *Lipids.* Negative results of tests with sudan III, sudan black and nile blue sulphate. Observation of the granules in polarized light did not reveal birefractive images.

(2) *Nucleic acid.* Feulgen's nuclear reaction and the ribonuclease digestion test gave negative results. The granules displayed a certain degree of acidophilia after ribonuclease treatment.

(3) *Polysaccharide.* Periodic acid and fuchsin-sulphurous acid treatment (Hotchkiss's test) indicates absence of detectable polysaccharides in the granules.

(4) On phase contrast microscopy, the granules appear dark, with regular outline and various diameters; they occupy the cytoplasma portion of the cell, leaving the zone occupied by the nucleus quite free; they also display poor Brownian movement.

(5) On vital staining with brilliant cresyl blue, the granules all stain blue, and none become yellow. The granules are partially and weakly stained with nile blue; there is no tendency to metachromatic staining.

(6) Toluidine blue tests reveal that the granules have a strongly metachromatic character (acidophilia).

Various hypotheses can be formulated with regard to the nature of granules.

(*a*) They might indicate cellular suffering caused by possible toxic action on the part of lysozyme. (*b*) Lysozyme treatment may reveal pre-existing formations in the cytoplasm. For example, it might be considered that the basic lysozyme cytoplasm links up with certain protein acids in the cytoplasm. (*c*) Particular differentiated structures in the cytoplasm, such as mitochondrial or ergatoplasmic formation, may be revealed.

Carlo Callerio
Istituto di Ricerche Terapeutiche Alexander Fleming,
via Modica, 6,
Milan.
April 28.

BIOLOGY

Transport of Driftwood from South America to Tasmania and Macquarie Island

In February 1955, a log about 10 ft. long and 5 ft. in girth was found washed up on a sandy beach just inside Port Davey harbour on Tasmania's south-west coast. It was lying between two logs of Huon Pine (*Dacrydium franklinii* Hook f.), an endemic conifer of Tasmania. Unlike these logs which were well covered with marine growth it was free from such growth although the surface was 'woolly' with many pebbles embedded in it. The ends of the log were sawn and one end grooved for towing by a wire rope. The wood was identified from its anatomy as a species of *Nothofagus*, which genus is represented in Tasmania, the south-eastern portion of the Australian mainland, New Zealand, New Guinea, New Caledonia and South America[1]. Anatomically the genus can be divided into two easily distinguishable groups, the one covering the species of New Guinea and New Caledonia, and the other the remaining species[2]. The log in question was derived from the second of these two groups and, because of the presence of spiral thickenings in the vessel elements, its specific identity could be narrowed down to one of three possibilities, namely, *N. moorei* (F. Muell.) Krasser of northern New South Wales and south-eastern Queensland, *N. pumilio* (Poepp. and Endl.) Krasser and *N. obliqua* (Mirb.) Oerst. from South America. The spiral thickenings in *N. moorei* differ from those of the two South American species; those of the unknown resembled the thickenings observed in the South American species. Both *N. pumilio* and *N. obliqua* are restricted to South America, the former occurring from Tierra del Fuego north to latitude 36° S. on the western side of the Andes. *N. pumilio*, *N. antarctica* (Forst.) Oerst. and *N. betuloides* (Mirb.) Oerst. are logged commercially in the southernmost tip of the continent[3]. All the anatomical evidence thus pointed to a South American origin of the log in question although this conclusion met with some initial opposition.

We have found no reports in the literature of driftwood travelling over such long distances (10,000 miles). Cockayne[4] mentions in passing that logs are carried from New Zealand to the Chatham Islands, a distance of 500 miles. Matthews[5] states that the fjords of the west coast of South Georgia contain large quantities of driftwood much of it from wrecks but some consisting of "the trunks and limbs of several trees, one with root stumps at the butt". Matthews concludes they must have drifted from where they grew "for no one would have brought such crooked, useless timber across the ocean". The nearest source would be Tierra del Fuego, about 1,000 miles away. The Australian National Antarctic Research Expeditions[6] to Macquarie and Heard Islands have also reported gnarled driftwood on the beaches of these islands which, like South Georgia, are devoid of native trees.

A request for samples of driftwood from Macquarie Island brought twenty specimens collected by the 1957 party on the west coast, and one, from a large log on the south coast, collected by the 1958 party. All have been identified anatomically. The original twenty consisted of twelve hardwoods, seven softwoods, and one piece of bamboo. All the hardwoods were identified as belonging to the genus *Nothofagus* and seven of these had the well marked spiral thickenings in the vessels characteristic of the South American species *N. pumilio* and *N. obliqua*; other anatomical evidence pointed to *N. pumilio*[3]. The specimen from the large log, collected by the 1958 party, was also identified as probably *N. pumilio*. Only one log was sawn at both ends; the others had no saw or mill marks. The notes accompanying the specimens and the photographs supplied indicated that the logs varied in length from 1 ft. to 15 ft. and from 4 in. to 30 in. in diameter. One (Fig. 1) was a split boomerang-shaped piece and another had root bases protruding at one end. Of the five specimens without spiral thickenings the notes record

Fig. 1. Boomerang-shaped piece of driftwood from the west coast of Macquarie Island identified as *Nothofagus* ? *pumilio*; this appears to have been derived from a large limb. The piece was 4 ft. long, 6 in. tapering to 4 in. in diameter. (*Photo. by H. Black*)

that two of the logs were sawn and that the other logs ranging from 5 to 10 ft. in length and from 2½ to 7 in. in diameter were not sawn.

There seems little doubt that this collection of specimens has been transported by ocean currents. It would seem most unlikely that some of the pieces had been taken on board ship, even as firewood, although the sawn logs could conceivably have been transported by ship. Eight of the logs were derived from species growing naturally only in South America, 10,000 miles from Macquarie Island, and there is little, if any, commercial traffic in these species outside Chile and Tierra del Fuego. The other five could also have originated from South America. The set of currents in the 'roaring forties' makes their origin from Tasmania or New Zealand most unlikely.

Of the seven softwoods five were identified as spruce (*Picea* spp.) a genus restricted to the northern hemisphere north of latitude 36° and, as far as we are aware, not planted on a large scale in the southern hemisphere. The logs were straight and varied in length from 5 to 15 ft. and in diameter from 2 to 10 in. Three had sawn ends; the largest and smallest were not sawn. It is possible that these logs were transported by a ship which was wrecked in southern latitudes but the variation in diameter makes this less likely. Large quantities of spruce are harvested and transported by water down the rivers on both the Pacific and Atlantic coasts of Canada and the Northern United States. Many must escape. Whether some combination of ocean currents would transport them to Macquarie Island must be left for future investigation. However, it is of interest to note that Heyerdahl[7] has reported the preference of the Hawaiians in the past for drift logs of Douglas fir (*Pseudotsuga menziesii* (Mirb.) Franco) for the construction of their ancient canoes.

The remaining two conifers were of the genus *Pinus*; both were derived from logs 9 in. in diameter. One was identified as belonging to the southern pine group (for example, *Pinus taeda* L., *P. palustris* Mill., etc.) the other to the white pine group (for example, *P. monticola* Dougl., *P. strobus* L., etc.). The natural distribution of this genus is restricted to the northern hemisphere but many species are widely planted in Australia, New Zealand and Chile. However, representatives of the above two groups are not the ones most commonly used. Thus the chances of these two conifer specimens having their origin in the southern hemisphere are remote.

This small collection of driftwood thus has a most varied geographical origin. There seems little reason to doubt that the *Nothofagus* specimens have drifted from Tierra del Fuego (longitude 70° W.) to Macquarie Island (longitude 160° E.) and the west coast of Tasmania (longitude 146° E.) in the track of westerly winds. Sverdrup *et al.*[8] give the speed of the surface current in the Antarctic circumpolar drift as 15 cm./sec. Using this figure, the time taken for a log to drift from South America to Macquarie Island would be over 3 years. This represents a maximum estimate of the time for the voyage, since, if any part of the log projects from the water, it will be 'sailed' through the water by the westerly winds. However, it is interesting to mention that a message bottle dropped about 1,250 miles to the west of Macquarie Island was recovered from the beach of that island 10 weeks later, giving a surface speed of, at least, 33 cm./sec.

It is strange that all the hardwoods found and examined have proved to be *Nothofagus*. This may be an accident of sampling but is due, more probably, to the fact that in the extreme southern latitudes of South America *Nothofagus* forms almost pure stands. It is hoped to obtain further samples of driftwood from Atlantic and Pacific Islands in southern latitudes. In this connexion it is of interest to record that two such specimens have already been received from Tristan da Cunha (12° W.) in the south Atlantic and both have been identified as *N.* ? *pumilio*.

Determinations of air-dry density on various samples of *Nothofagus pumilio* have given values around 32–35 lb./cu. ft. In this respect, therefore, they are little heavier than most of the conifers including species of *Pinus* and *Picea*.

The bearing of these results on the problem of the floristic botany of the southern continents will be discussed elsewhere. However, it does not seem impossible for seeds to be overgrown in the wood or, as Darwin observed[9], trapped and sealed into the interstices of the roots and then transported from one continent to another. This remote chance which has presumably been available for the 100 million years since the origin of the Angiosperms may be part of the explanation of the puzzling floral similarities of the southern tips of the continents.

We wish to acknowledge the help provided in collecting specimens by the officers of the Australian National Antarctic Research Expeditions, in particular Mr. Harry Black, Officer-in-Charge of the 1957 party at Macquarie Island, and by Mr. D. H. Simpson, Agricultural and Forestry Superintendent, Tristan da Cunha. We also wish to thank Mr. W. L. Davies of the Geography Department, University of Tasmania, for his help in discussing these problems of geography.

H. N. Barber
H. E. Dadswell
H. D. Ingle

Department of Botany,
University of Tasmania,
and Division of Forest Products,
Commonwealth Scientific and
Industrial Research Organization,
Melbourne.

March 31.

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Sterility in *Lathyrus odoratus* L.

Male sterility in *Lathyrus odoratus* L. was first recorded by Bateson, Saunders and Punnett[1]. Male sterility was absolute and was inherited as a single recessive gene linked to light axil and cretin[2]. Fabergé[3] and Upcott[4] reported that the sterility resulted from disturbances in the meiotic division following normal metaphase pairing. Such plants were normal and fully fertile on the female side.

Table 1

	No. of crosses or selfs	Pods with seed	Total seed	Mean seed per pod	Mean seed per pollination
Controlled self-pollinations					
(*a*) Fertile plants	54	29	127	4·4	2·3
(*b*) 'Sterile' plants	50	0	0	0	0
Crosses between fertile and 'sterile' plants					
(*a*) Fertile as ♀	52	10	22	2·2	0·42
(*b*) 'Sterile as ♀	50	0	0	0	0

during prophase (Fig. 1), metaphase was characterized by complete asynapsis (Fig. 2). The chromosomes during the first division remained undivided and were randomly distributed into two or more groups. Each group of chromosomes behaved normally for the completion of the meiotic division, though seldom was a viable gamete produced, as few of the first division segregations were genomically reductional. The cytological behaviour of this asynaptic form of *L. odoratus* closely resembled the observations reported by Blakeslee *et al.*[5] for the asynaptic variant of *Datura*.

Segregation ratios from heterozygous material suggest that this asynaptic sterility is controlled by a single recessive gene.

J. R. Ellis

Department of Horticulture,
Purdue University,
Indiana.

M. A. Burton

Department of Botany,
University of Manchester.

April 27.

Sterility affecting both male and female gametes has recently been observed in an unnamed blue-flecked variety of the sweet pea. (Seed of this variety was supplied by Mr. D. G. Taylor of the Cheshire School of Agriculture.) The anthers contained a small amount of stainable pollen (5 per cent) which rendered them partially fertile as male parents. Table 1 shows the results of self and cross pollinating fertile and 'sterile' plants. From many hundreds of flowers on the 'sterile' plants, one pod set (from an uncontrolled pollination) containing two seeds. Hence sterility was almost complete on the female side and high on the male side. Cytological observations of the meiotic division in the pollen mother cells showed that although normal pairing occurred

Fig. 1. Meiotic prophase showing chromosome pairing as evidenced by (1) small impaired region, *A*, and (2) probable inversion loop, *B*. (× 1,500)

Fig. 2. Metaphase 1 showing 14 unpaired chromosomes. (× 1,500)

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Tolerance to Skin Homografts of Adult Mice after Parabiosis

Skin grafts between mice of different inbred strains are invariably rejected within a few weeks. Hybrid (F_1) tissues transplanted to mice of either parental strain are also consistently rejected at the same rate if the parents differ at the *H*-2 histocompatibility locus[1]. This uniform incompatibility was not apparent when such hybrids were united in parabiosis with parental strain inbred mice. The most frequent result of such unions was the death of only the hybrid partner, usually within a month. Hybrid death in this period was characteristically preceded by a severe wasting disease, sometimes described as 'parabiotic intoxication'[2].

The variability of survival time of the parabiotic unions between different strain combinations is shown in Table 1. The F_1 hybrids were all crosses between inbred mice of different *H*-2 genotypes. All animals were of the same sex and 2–3 months old when united. The parabioses that persisted beyond 60 days were eventually terminated by the 'natural' death of both partners without manifestations of the wasting disease.

Of the combinations tried here, the parabiosis of the $(C3H \times DBA/2)F_1$ hybrids with *DBA*/2 inbred mice

Table 1. Survival Times of Parabiotic Unions between Inbred Strains of Mice and their F_1 Hybrids of the same Sex and Age (2–3 Months)

Combination in parabiosis	No. of pairs done	Pairs surviving beyond 60 days	Death of hybrids Time in days	
			Average	Range
$(C3H \times DBA/2)F_1$—*DBA*/2	71	29	19·7	13–31
$(R1(1 \times DBA/2)F_1$—R1II	6	0	14·8	12–16
$(R1II \times C3H)F_1$—R1II	8	1	16·1	14–21
$(C57BL \times C3H)F_1$—*C57BL*	12	0	26·1	8–52
$(A \times C3H)F_1$—*A*	17	0	20·2	9–31
$(DBA/2 \times NH)F_1$—*DBA*/2	4	1	23·0	14–33

provided the most frequent stable unions. Fourteen such pairs that were not treated further survived in stable parabiosis for periods lasting 80–510 days. The two successful parabioses among other strain combinations in Table 1 survived 310 and 85 days.

Parabiotic pairs that had been together for about five months were used for the first skin grafting experiment (Table 2, Group 1). The full thickness skin of young $(C3H \times DBA/2)F_1$ hybrids were grafted to each of the five $DBA/2$ mice still in parabiosis. The grafts were all successful. Three months later the skin of inbred *C3H* mice was placed adjacent to the earlier grafts. These were also uniformly successful, in spite of the major histo-incompatibility between the two inbred strains. Approximately two months later (10 months after parabiosis) all of the unions were surgically terminated. The host $DBA/2$ mice survived up to six months after the termination of parabiosis with all the grafts still in place. In the next experiment (Table 2, Group 2), 3$DBA/2$ mice in parabiosis for 5 months were grafted only with *C3H* skin. A soon as the skin was well established, the parabionts were cut apart. After another 2–3 months the grafts began to contract slowly, disappearing 3–4 months after the termination of parabiosis.

Table 2. Results of Graft ng *C3H* and $(C3H \times DBA/2)F_1$ Skin on $DBA/2$ Mice after Parabiosis with $(C3H \times DB\ 1/2)F_1$ Hybrids of the same Sex and Age (2–3 Months)

Group	No. of mice	Days after parabiosis at which indicated events occurred: Experimental: Skin graft while in parabiosis	Experimental: Parabionts separated	Experimental: Skin grafts (*C3H*) after separation	Results: Slough	Results: Dead
1	5	162–165 (F_1), 224–228 (*C3H*)	307	none	no	418–488
2	3	126–130 (*C3H*)	176	none	208–317	no (>400)
3	1	none	306	401	no	446
4	2	none	154	209	no	no (>270)
5	2	none	82	98	144–171	no (>270)

In the following three groups (Table 2, Group 3–5), the *C3H* skin was successfully grafted on $DBA/2$ mice after the parabiosis with the hybrid had already been terminated. In one instance an initial *C3H* skin graft was accepted three months after separation of the parabionts. However, when the total period of parabiosis was just 82 days, compatibility lasted for only 2–3 months after the surgical parting. In other cases, where parabiosis had been allowed to persist for 5 months, the subsequent period of compatibility is continuing after 4 months.

It should be pointed out that in no case has a graft of *C3H* or $(C3H \times DBA/2)F_1$ skin on untreated $DBA/2$ control mice shown comparable compatibility. More than 100 such control animals always rejected these homologous skin grafts within 3 weeks and never showed the full regrowth of hair that was characteristic of the good acceptance of *C3H* skin in the parabiosed $DBA/2$ mice.

When $(C3H \times DBA/2)F_1$ hybrids died by the wasting disease during the early weeks after the parabiosis, the surviving $DBA/2$ partners were tested for their reaction to grafts of *C3H* skin. In these cases, the outcome was a typical 'second set' reaction, the rapid and violent rejection of the foreign skin. Evidently antibodies were already present when the skin homograft was presented. Other recent evidence[3–4] indicates that the 'wasting disease' syndrome, as seen in the hybrid, is the consequence of an immunological reaction of parental strain lymphoid elements against hybrid tissues. The reverse cannot occur; the hybrid does not produce antibodies to parental strain tissue. Therefore, as expected, the wasting disease was never seen in the parental strain in parabiosis with its hybrid.

The present observations may perhaps be interpreted in the context of other studies[5,6], where the injection of blood and minced tissues create 'enhancement' of transplantation, rather than immune rejection. The deciding factor in these experiments seems to be the quantity of antigen and the mode of injection. While small inocula given subcutaneously provide immunity and rejection, large amounts given intravenously may do the opposite—promote tolerance. In this light, the rejection of homografted skin may be considered the result of a small antigenic stimulus by the graft itself, while the occurrence of successful parabiosis is always preceded by the continuous intravenous exchange of large amounts of antigen. Only after such successful parabiosis was tolerance to homotransplantation demonstrable.

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B. A. Rubin

Department of Virology and Epidemiology,
Baylor University College of Medicine,
Houston, Texas.
May 5.

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Common Attractant for the Tobacco Hornworm, *Protoparce sexta* (Johan.) and the Colorado Potato Beetle, *Leptinotarsa decemlineata* (Say)

The specificities of oligophagous insects to groups of related plants have been postulated and demonstrated in several instances to be mediated by secondary plant substances of limited distribution (reviewed by Dethier[1] and Fraenkel[2,3]). These substances are variously called attractants, token stimuli, or phagostimulants when they serve in such capacity and are generally tested on the feeding stages of the insects concerned by applying the substances on various artifices such as filter paper, pith disks, non-host leaves or agar gel diets. The insects are then allowed to discriminate the presence of the attractants by biting or feeding.

The function of specific substances in the feeding

behaviour of the Colorado potato beetle, *Leptinotarsa decemlineata* (Say) has recently been a centre of interest in many laboratories, especially in France, Germany, and the U.S.S.R. (see, for example, the report of the symposium on "Insect and Foodplant" held at Wageningen[4]). While most of the relevant work deals with the identity and function of glycoalkaloids in Solanaceae as factors of repellency or toxicity, the nature of the specific attractant has commanded little attention. Hesse and Meier[5] claimed acetaldehyde as the specific attractant; but this claim was not substantiated by later workers. Earlier, Chauvin[6] reported the isolation from potato leaves of an attractive substance which was tentatively identified as a flavone glycoside. The technique was improved later[7] and the attractiveness of the substance was confirmed by Thorsteinson[8]. During an investigation of the oligophagous habits of the tobacco hornworm, *Protoparce sexta* (Johan.), which also feeds on members of the same family of plants, Solanaceae, a glycosidic substance attractive to this insect was isolated from several plants including tomato and potato[9]. We had an opportunity to assay this material on filter paper against the Colorado potato beetle, and found that the material was also highly attractive as a feeding stimulant for the beetle (Fig. 1).

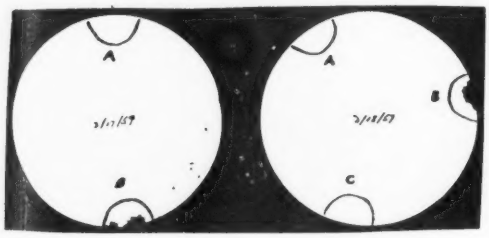

Fig. 1. Biting responses to the attractant purified from tomato leaves by the Colorado potato beetle (left) and the tobacco hornworm (right). *A* and *C* on the filter paper are control spots on which 0·01 *M* of sucrose was applied; *B* represents test spots on which a solution of the attractant was applied

The chemical identity of this substance has not been elucidated as yet; but preliminary characterizations indicate that it is not a flavonoid derivative. In our experiments, flavonoids were removed before subsequent purification, and hence the flavone glucoside claimed by Chauvin as the active substance for the Colorado potato beetle might have been present in his preparation as an impurity. The results of our bioassay strongly suggest that the specific attractant for the potato beetle and tobacco hornworm is identical.

ROBERT T. YAMAMOTO
G. FRAENKEL

Department of Entomology,
University of Illinois,
Urbana, Illinois.
April 7.

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GENETICS

Simultaneous Change in Both Differential and Interference Distances of Chiasmata

On the basis of a serial formation of chiasmata in time beginning from the centromere, the effect of experimental factors on chiasma formation has been interpreted in terms of the two parameters, differential and interference distances[1–3]. By differential distance is meant the distance of the first chiasma from the centromere, and by interference distance, the length of the chromosome arm between the successive chiasmata. With a change in the differential distance alone, the graph showing the relation between chromosome length (x) and chiasma frequency (y) has a series of parallel lines for different temperatures, intersecting the line $y = 1$ at their respective differential distances (Fig. 1*a*). Mather[3] interprets White's results[4] from temperature experiments as showing this type of effect. On the other hand, if only the interference distance changed, the different lines would radiate from the same point (Fig. 1*b*). Mather[3] again explains the data of Moffett[5] on different individuals of *Culex* as representing this type of change. Apart from these examples by Mather which have become classical in studies on chiasma frequency, there does not seem to have been any other interpretation of results along such lines. Data was therefore extracted from experiments of mine[6,7] which had shown that temperature reduced chiasma frequency per pollen mother-cell in the bluebell, *Endymion nonscriptus* (L) Garcke.

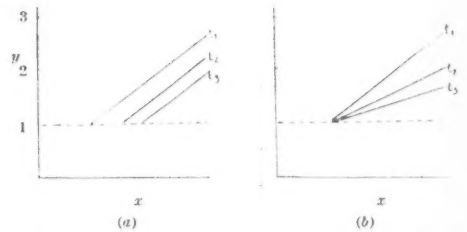

Fig. 1. (*a*) Graphical representation of chiasma frequency–chromosome length relationship when there is a change in differential distance only. (*b*) Graphical representation of chiasma frequency–chromosome length relationship when there is a change in interference distance only

The data for the present study came from three clones (C_5, C_6, A_{18}), two of which consisted of two individuals each and the third one of three individuals.

The two plants of each of clones C_5 and C_6 were placed at temperatures of 10° and 25° C., and the three plants of clone A_{18} at 0°, 10° and 25° C. It is not possible to give the full results here; they will

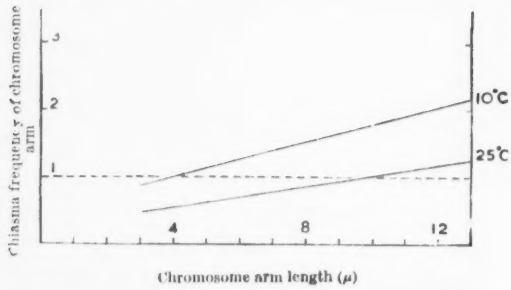

Fig. 2. Regression lines for relation between chromosome length (long arms of the complement) and chiasma frequency at 10° and 25° C. (in clone C_5) in the bluebell, *Endymion nonscriptus*

be published elsewhere. They consisted of the mean chiasma frequency of each bivalent as well as its component arms in each of the plants under study (see also ref. 6). The present studies were confined to the long arms of the chromosome complement since they could each form more than one chiasma.

The graphs showing the relation between chromosome length in microns (x) and chiasma frequency (y) for each plant at a particular temperature were constructed from corresponding calculated regression lines between (x) and (y) as described below.

Clone C_5. At 10° C. the regression coefficient b was 0·1264 which was highly significant, $F = 20{\cdot}5869$ ($P < 0{\cdot}001$); at 25° C., b was 0·07276, also significant, $F = 18{\cdot}3367$ ($P < 0{\cdot}001$). The calculated regression lines are shown in Fig. 2. The two lines are clearly separated from each other and they have different slopes. They would be expected to be parallel if there was only a change in differential distance.

Clone C_6. At 10° C. the regression coefficient b was 0·13601 which was highly significant, $F = 17{\cdot}37465$ ($P < 0{\cdot}001$); at 25° C., b was 0·11058, also highly significant, $F = 22{\cdot}6005$ ($P < 0{\cdot}001$). The calculated regression lines are similar to those for clone C_5 in showing not only a change of position but also of slope. In fact, they seem to combine parallel and 'radiating' lines at the same time as one would expect with a change in both differential and interference distances.

Clone A_{18}. This clone with three plants was examined for this relationship 0°, 10° and 25° C. The regression coefficient was significant ($P < 0{\cdot}001$) at each temperature (at 0° C., $b = 0{\cdot}11297$, $F = 25{\cdot}4306$; at 10° C., $b = 0{\cdot}11489$, $F = 36{\cdot}5462$; at 25° C., $b = 0{\cdot}11175$, $F = 76{\cdot}1858$). The calculated regression lines show a much smaller change in slope than those for clones C_5 and C_6, but the change is still clear. This could be inferred from the similarity in the regression coefficients at the three temperatures in clone A_{18}, and is probably also due to the relatively smaller decrease in chiasma frequency in this clone between the temperatures 10° and 25° C. as compared with those in clones C_5 and C_6. Thus it seems that in clones C_5 and C_6, and A_{18}, both the differential and the interference distances have been altered by temperature.

Further examination was made of the long arms of the long chromosomes. Since there seems to be a better correlation between chromosome length and chiasma frequency of the long chromosomes in a varied chromosome complement than of the shorter ones[3], the long arms of chromosomes A, B, C and D, which could each form up to three chiasmata, were used directly in plotting a relationship between their lengths in microns and chiasma frequency at 10° and 25° C. From these it is clear that the same sort of relationship of the two lines is obtained by this direct plotting, that is, the lines show clearly not only a change of position but also of slope.

The present results suggest a simultaneous change in both the differential and interference distances with changing temperature. A case of this joint change does not seem to have been predicted or reported. The examples given by Mather[3] deal only with an independent change in either parameter.

J. Yanney Wilson

University College of Ghana,
Achimota.
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Anomalous Genetic Interactions observed in *Bacillus subtilis*

Genetic transformation in *B. subtilis* has recently been reported by Spizizen[1], but as yet no paper has appeared discussing genetic interaction between the cells of spore-bearing bacteria. In this communication, a new fact will be described which was discovered while attempting to cross auxotrophic mutants of *B. subtilis* K. It involves the *de novo* appearance of characters not present in the parent strains. The complete details of this work will be published elsewhere.

Two mutants were employed: *T*16—try, ade, str-r (requiring tryptophan and adenine, and streptomycin-resistant), and *M*12—met, his, str-s (requiring methionine and histidine, and streptomycin-sensitive). These biochemical mutants were obtained after exposure to X-rays, and the streptomycin-resistant strain was obtained by Szybalski's agar-gradient method.

The mutants were cultivated in nutrient broth at 30° C. until the cell density reached about 10^8/ml. Centrifuged cells were washed once with phosphate buffer and the cell suspensions were plated in mixture on synthetic media supplemented with various nutrients (see Table 1). After four days at 37° C. a considerable number of tiny colonies appeared on the supplemented media, but nothing appeared on the minimal medium. In general, the tiny colonies were analysed by spreading cell suspensions prepared by homogenizing the colonies in a small blendor on various media.

Table 1. Frequencies of Tiny Colonies

No. of cells plated	No. of tiny colonies appearing on THS	TMS	MHS	MM
*T*16 + *M*12 6×10^7 $1{\cdot}9 \times 10^7$	14	8	44	0
Frequencies	$1{\cdot}6 \times 10^{-7}$	$9{\cdot}1 \times 10^{-8}$	$5{\cdot}0 \times 10^{-7}$	—

Total cell number was determined on nutrient agar. It was impossible to count tiny colonies on MAS and HAS on account of the rapid growth of back mutants.

MM, Gray and Tatum's agar medium; THS, MM plus tryptophan 50 γ/ml., histidine 50 γ/ml. and streptomycin 100 γ/ml.; MHS, MM plus methionine 50 γ/ml., histidine and streptomycin; TMS, MM plus tryptophan, methionine and streptomycin.

(1) *The occurrence of a met, his, ura, str-r strain.* Five tiny colonies which appeared on THS medium were subcultured on the same medium. After 2 days the cells resulting from each tiny colony were analysed. In all cases, both try, ade, str-r, and met, his, ura, str-r progeny were obtained (for example, one tiny colony consisted of 13×10^7 try, ade, str-r, and 205×10^5 of met, his, ura, str-r). In another experiment, which was repeated from the beginning, the met, his, ura, str-r progeny were again obtained from the cell suspension which was prepared directly from a tiny colony, but this time try, str-r progeny were recovered instead of try, ade, str-r. The appearance of the met, his, ura, str-r type is of particular interest, because the requirement of uracil for growth is a new character which did not exist in the parental strains.

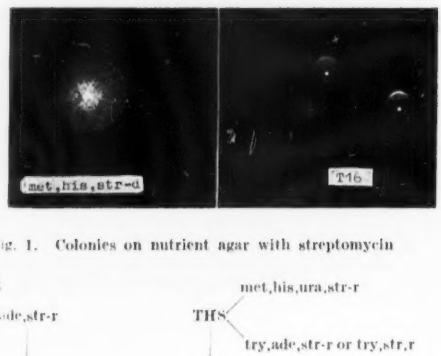

Fig. 1. Colonies on nutrient agar with streptomycin

* Phenotypic expression.
Fig. 2. Progeny of tiny colonies

(2) *The occurrence of streptomycin-dependent strains.* One of the tiny colonies on MHS was analysed by spreading a cell suspension on various media. It was found that the colony consisted of a large number of try, ade, str-r (335×10^3), and a small number of try, str-r cells (133×10^1): nothing was observed on MH medium. Despite the fact that no colonies appeared on MH medium, a considerable number of colonies (153×10^1) did appear on MHS medium. These colonies behaved as follows: (*a*) the cells grew on MHS, TA and nutrient agar but not on MH medium; (*b*) cells grown on TA or nutrient agar yielded no colonies on MHS medium; (*c*) the morphology of the colonies on nutrient agar with streptomycin was different from that of *T*16 (Fig. 1), and they could grow on MHS but not on TA or TAS media; but when one of them was cultivated in nutrient broth supplemented with streptomycin they segregated out try, ade, str-r progeny with a frequency of 10^{-3}; (*d*) no streptomycin-sensitive progeny were obtained at all.

These facts (see Fig. 2 for summary) indicate that the streptomycin-dependent cells, when subcultured on MHS medium, maintain the potentiality to segregate try, ade, str-r progeny. This phenomenon may be explained by the assumption that the streptomycin-dependent progeny consisted of single cells which had a whole chromosome of *T*16 and a fragment of *M*12 at the same time. But the two genetic units might not fully complement one another.

A similar genetic interaction between two types of genome was reported by Bradley in *Str. coilicolor*[2].

M. Kohiyama
Y. Ikeda

Institute of Applied Microbiology,
University of Tokyo.
April 1.

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GEOGRAPHY

Evidence of a South Equatorial Countercurrent in the Pacific Ocean

An eastward-flowing current of speeds from 10 to 25 cm./sec. is indicated along a density surface ($\sigma_t = 26{\cdot}81$) in the Pacific Ocean south of the equator in a position roughly symmetrical to that of the (North) Equatorial Countercurrent. Along this surface the current is found between lat. 2° S. and 5° S. at long. 165° E. and progressively farther south toward the east, to between lat. 10° S. and 14° S. at long. 95° W. The depth of this surface rises to the south along the flow, from 400 to 300 m. in the west and from 400 to 350 m. in the east.

The evidence lies in the calculations of geostrophic flow along this surface with respect to 1,000 decibars[1]. The eastward geostrophic flow is indicated on ten cross-sections made by the *Equapac* expeditions (joint surveys carried out by agencies from France, Japan and the United States) in late summer of 1956, on three sections made by the *Carnegie* cruise of 1929–30, ref. 2, and by combinations of stations from the *Carnegie*, *Eastropic*[3,4] and *Downwind* (Univ. of Calif. Scripps Inst. of Oceanogr., unpublished reports) expeditions.

On this surface the path of the eastward flow coincides with a tongue of high salinity extending eastward from a maximum value in the Coral Sea.

North of the equator the (North) Equatorial Countercurrent is indicated on the same density surface by calculations of geostrophic flow. The depth of the surface rises to the north from more than 400 m. at the equator to a ridge of depth less than 300 m. at lat. 5° N., long. 135° E. The ridge extends eastward to lat. 10° N. long. 145° W. at less than 300 m. It continues from there to lat. 5° N.,

long. 115° W., where its depth is about 350 m. The eastward flowing current is evident on this surface between lat. 2° N. and 5° N. in the west, from lat. 4° N. to 8° N. in the central ocean, and from lat. 5° to 10° N. at long. 120° W., and is indicated on all of the *Equapac* sections and the pertinent *Carnegie* and *Eastropic* sections all the way to the coast of America. Direct measurements[4] made recently in the eastern Pacific have revealed that the eastward flow extends to at least 1,000 m. at long. 107° W.

There is evidence of an eastward flow at the sea surface south of the equator in the measurements of geostrophic flow made on the *Equapac* expeditions by the research vessels *Orsom III* (Institut Français d'Oceanie, New Caledonia, unpublished report) at lat. 9° S. between long. 170° and 180° E., where speeds as high as 15 cm./sec. are indicated, and by the *Hugh M. Smith*[5] at the same latitude between long. 169° W. and 135° W., with speeds as high as 8 cm./sec. indicated. Of the other *Equapac* lines, none reached so far as lat. 10° S. except one at long. 164° by the *Horizon* (Univ. of Calif. Scripps Inst. of Oceanogr., unpublished reports) and this was so near the Solomon Islands that the geostrophic calculations, which did indicate an eastward flow, might have other interpretations.

In a combination of stations from the *Carnegie* expedition and the *Eastropic* expeditions of 1955 and the *Downwind* expedition, a weak easterly flow may be interpreted so far east as long. 95° W., but the observations are sparse and the feature is very poorly defined.

In the western Pacific, other evidence for the eastward flow at the sea surface may be found in various atlases prepared from observations of set and drift of vessels. The British average[6] of set and drift for the seasons November–January and February–April indicate a weak eastward flow at lat. 10° S. from long. 165° E. to 140° W. and from long. 165° E. to 165° W., respectively. No evidence is found in other months, and it is to be noted that the *Equapac* observations were made in August. The more recent Netherlands[7] monthly current charts show easterly flow along lat. 10° S. from long. 165° to 180° E. in February, March and April. The American[8] monthly charts show almost no evidence in any month.

The east-flowing current was encountered while studying the distribution of temperature, salinity, and oxygen along the density surface σ_t 26·81, which lies in the intermediate water in the North Pacific and above the intermediate water of the South Pacific. This study is not yet completed, and further information about the flow at other depths and along other surfaces will be obtained as the work progresses.

Joseph L. Reid, jun.

Scripps Institution of Oceanography,
University of California,
La Jolla, California.

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River Flow in Great Britain

Prof. D. L. Linton, in his article on "River Flow in Great Britain, 1955–56"[1], has a map showing 'run-off deficit', defined as "Precipitation minus run-off".

While believing that maps of this parameter are much needed, it is doubtful whether the data from which they can at present be constructed for Great Britain are sufficient for drawing isopleth maps with any degree of accuracy. The network of gauging stations is too thin for it to be possible to assume that known errors in measurement of run-off, and in assessing rainfall over a whole catchment area, can cancel each other out. The estimation of precipitation is likely to be the most unreliable in large catchment areas of high relief, and these areas happen in general to be where the river-gauging network is particularly thin. These errors can alone well account for the apparently anomalous high run-off deficits in the Scottish Highlands without necessarily invoking any other explanation.

Prof. Linton comments that the geographical variations of the fractions of precipitation disposed of by run-off and by evapo-transpiration are radically different, and adds: "it is doubted whether there has previously been any general appreciation of this difference by water engineers and others". There may not have been a "*general* appreciation" of this fact, but it has certainly been appreciated by some, who further appreciate that there is an important difference which is not revealed on his map, and which Prof. Linton does not mention, between different parts of the country. In fact of course the map, allowing for the errors mentioned above, does indicate the general geographical distribution of actual loss by evapo-transpiration; this however is in some parts of the country equal (in 1955–56, as in other years) to potential evapo-transpiration and in other parts not. In the rainfall year in question, the difference between actual and potential evapo-transpiration can safely be said to have been between 0 and 2 in. in many parts of western and highland Britain, while it almost certainly reached 12 in. in many parts of the south of England. Thus an 'actual loss' of 20 in. in Ross-shire (as shown on the run-off deficit map) would be a 'run-off deficit', with little or no 'water deficit' while a similar run-off deficit in the south of England would be accompanied by a water deficit of 12 in. It needs to be emphasized that 'water-deficit' is not the same as 'run-off deficit'; but values of both are needed, and there is need for a network of observations sufficient for both to be mapped. Consideration of both would reveal why there can be a high run-off deficit in the west Highlands, without any need to refer, as Prof. Linton does, to the large bodies of open water there; there are, after all, large bodies of open water in the English Lake District, which had a much lower run-off deficit on the 1955–56 map.

Although, as Prof. Linton points out, there is a lack of gauging stations on the western seaboard, it is possible to extrapolate the map of 'discharge ratio' to the west coast, through observation or estimation of potential evaporation.

F. H. W. Green

The Nature Conservancy,
19 Belgrave Square,
London, S.W.1.

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